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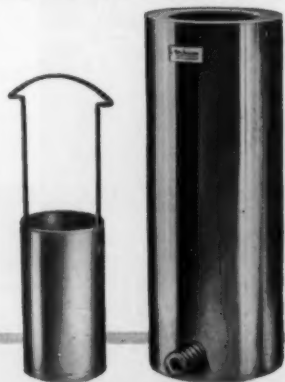


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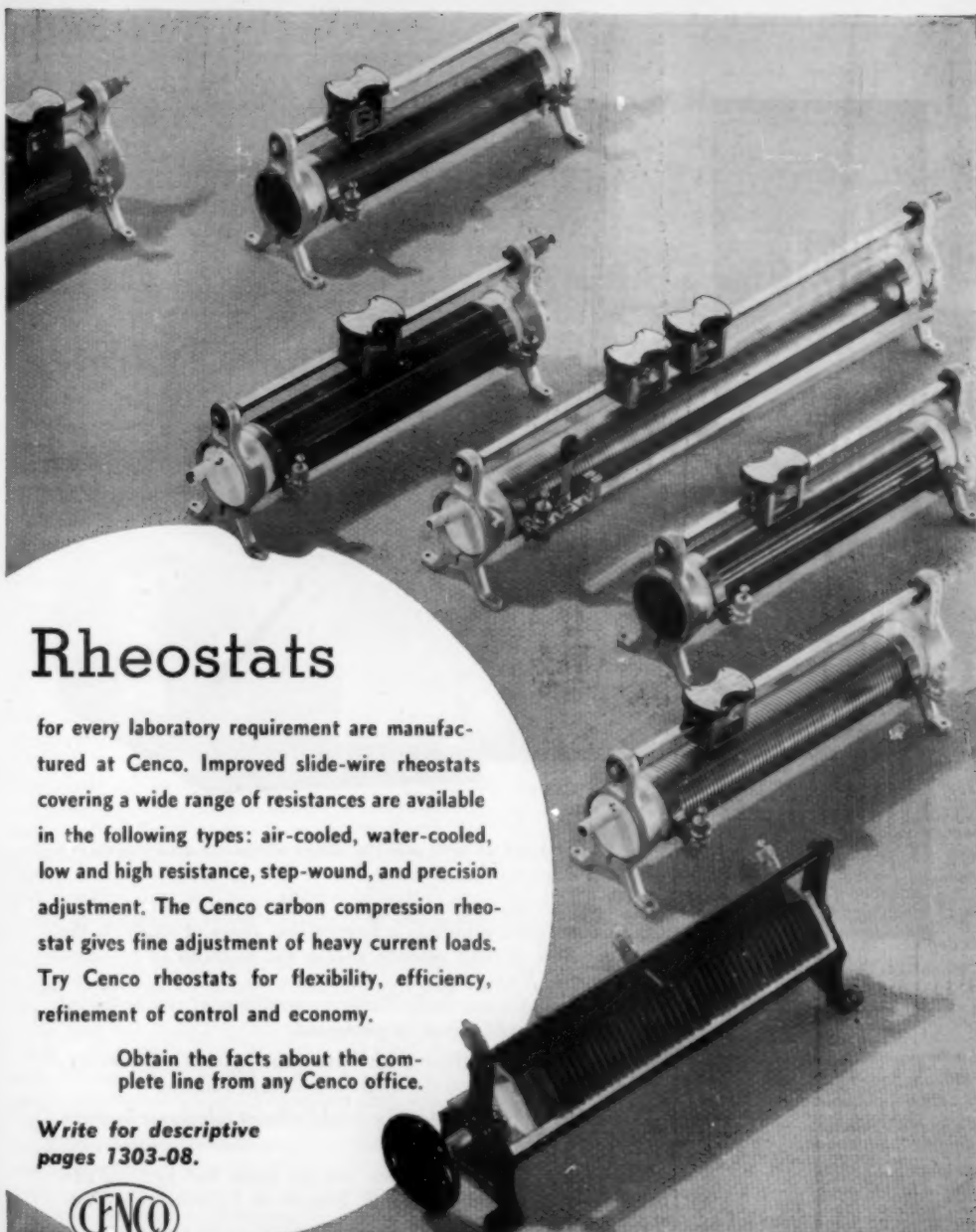
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A Century of Geography

THIS year the American Geographical Society is celebrating its hundredth birthday. During the past century it has grown from a handful of men interested in accumulating accurate knowledge of the earth to a large, independent research organization that employs more than 50 full-time staff members. Its specialized library now includes more than 150,000 publications, and its map library, the largest private collection in the Western Hemisphere, more than 250,000 maps and 3,000 atlases.

To celebrate its centennial year, the society is planning a number of special events. An exhibit, tracing its 100 years of activity, will be on display all during the summer months. In April a publication party is scheduled for John K. Wright's history of the society, *Geography in the Making* (cf. *Sci. Monthly*, 74, 121 [1952]). On May 22 the society will give a Charter Day party at its New York headquarters. August 4-6 it will play host to delegates from forty member-nations of the International Geographical Union, and awards will be presented to George B. Cressey, Maxwell professor of geography at Syracuse University and president of the Union; Roberto Almagna, professor of geography at the University of Rome and vice president of the Union; Carlos Delgado de Carvalho, director of the Brazilian Institute of Educational Research; and Gilbert Grosvenor, president of the National Geographic Society.

In 1952 the society is beginning a new project, which will include an educational program for schools and colleges, and a workshop to test and distribute maps, movies, globes, and periodicals that will help raise the level of geographical knowledge throughout the United States. A second project is that of publishing in cooperation with the Association of American Geographers a "National Atlas," to depict the land, life, and livelihood of America.

Nearing completion is a new map of North and South America, done on a scale of 1:12,500,000, and

drawn on a new projection (bipolar oblique conic conformal), which was devised by O. M. Miller. It is a direct descendant of the society's *Millionth Map of Hispanic America*, which took 25 years to complete. Consisting of 107 sheets, the Millionth Map was constructed by society geographers through cooperation of Latin American governments, corporations, and scientists. Six sheets of this map—which was completed in 1945—are being revised and brought up to date this year.

The Juneau Ice Field Research Project—the society's annual expedition to Taku Glacier in Alaska—will carry on its fifth year of investigations this summer. With a base camp now permanently established on a rocky island in the glacier's center, the society hopes to continue indefinitely its study of glacial movements and their relation to climatic changes.

The Medical Geography Department, established four years ago, is producing medical maps at the rate of four a year. It is planned to publish a comprehensive "World Atlas of Diseases," and five maps have already been completed—on Poliomyelitis, Cholera, Malaria, Helminthiasis, Yellow Fever, and Dengue.

In addition to Dr. Wright's history of the society, two other books are scheduled for publication in 1952: "Land for Tomorrow: The Underdeveloped World," by L. Dudley Stamp, to be published jointly with the Indiana University Press; and "Agricultural Origins and Dispersals," by Carl O. Sauer. A third book—"An Introduction to Photogrammetry," by O. M. Miller—is in preparation.

The society had its beginnings in an age of discovery and exploration, but it is increasingly devoting its energies to new types of exploration—the study of man-land relationships. This modern program was inaugurated in 1915 by Isaiah Bowman and has continued under the direction of John K. Wright and George H. T. Kimble to seek "new horizons in a shrinking world."

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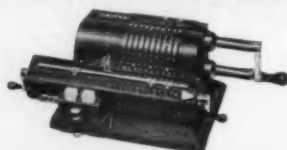


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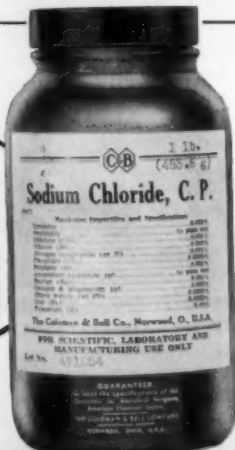
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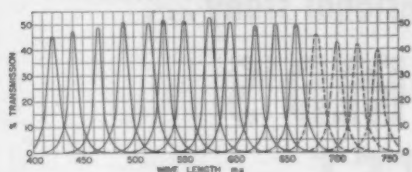
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The Support of Research in Medical and Allied Fields for the Period 1946 through 1951

Stella Leche Deignan and Esther Miller

*Medical Sciences Information Exchange, Division of Medical Sciences,
National Research Council, Washington, D. C.*

Foreword: One of the difficult tasks in human affairs is the establishment of joint enterprises designed to serve a number of groups. This is particularly true within the federal government, where the intricacy of the relationships within agencies makes interagency cooperative endeavors even more difficult. The Medical Sciences Information Exchange is such a cooperative endeavor. It was established in July 1950 within the Division of Medical Sciences, National Research Council, by six federal agencies, the Department of the Army, the Department of the Air Force, the Department of the Navy, the Atomic Energy Commission, the Public Health Service, and the Veterans Administration, which jointly support it and maintain it as a clearinghouse for information on grant and contract support in the medical and allied fields.

The Policy Committee, Medical Sciences Information Exchange, composed of the heads of the grant or contract divisions of the six agencies supporting the exchange, recognizes the contribution of the

many private philanthropic organizations whose cooperation in the exchange has made this report possible. The report is unique because it is a survey of a broad field of research—medical and allied fields. The cost of this research measured in dollars is great, and the number of individual projects is large. The maintenance of the project data on a current basis has resulted in substantial savings; it is hoped that its periodic summarization will effect additional economies in research administration.

The committee believes this report is an indication of the success of the cooperative effort. The daily use of the exchange by investigators throughout the country and by granting agencies is gratifying. With the publication of this report the exchange appears to have passed beyond the experimental stage. Its success breeds a hope that the procedure can be repeated in other fields of science.

THE POLICY COMMITTEE

Medical Sciences Information Exchange

THIS REPORT, comprising an analysis of 12,923 research grants registered with the Medical Sciences Information Exchange during the period 1946-51, is based on research grants and contracts awarded by government and by the larger public and private foundations. We present the report as an answer to the many requests for information that are received by the exchange, and in the belief that it will illustrate the value of a central clearinghouse and thus stimulate additional participation in the exchange.

As a preface to the analysis, certain limitations of the data should be defined. Few awards made by industry, local foundations, or funds established solely for individual universities have been included. The data from government are, perhaps, more extensive than those from private agencies because of the completeness of records of Public Health Service grants and to the fact that awards made by public and private foundations may not comprise the full programs of these agencies. However, information on contracts made through government agencies other than the Public Health Service is likewise incomplete, with the result that a balance between the government and private sources of funds is approached.

The year 1946 has been chosen as the first year of the record because it represents a period following the end of the wartime support of medical research through the Office of Scientific Research and Development and the beginning of expanded government sup-

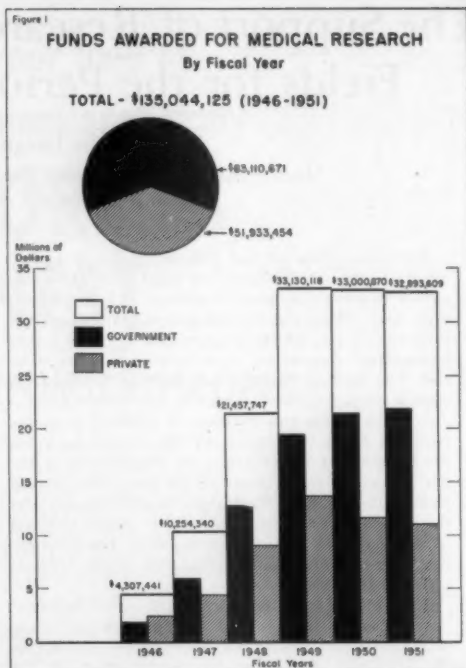
port of research on what was believed to be a peacetime basis. As an additional government or private agency began cooperation or fuller participation with the exchange, efforts were made to secure information on awards initiated as far back as the government fiscal year 1946, beginning July 1, 1945. There were some projects supported by private agencies during this period, the initial awards for which were made in earlier years and which were not, therefore, registered with the exchange. Any attempt to make our data complete for the period would have required surveys in such volume, and delays of such length, as to outweigh the value of the additional information secured. Our records for 1946 are, therefore, somewhat incomplete; furthermore, data for 1951 are limited because the material was compiled in the spring before the close of the fiscal year. Actually, the most complete year of the record is the fiscal year 1950. More than 500 additional grants registered with the exchange have been eliminated from this report because of a lack of information on the amounts awarded.

Throughout the report, the term "grant" is employed to mean an amount of money approved for the support of a project for the period of one year and refers to both grants and contracts. "Year" is the governmental fiscal year which begins July 1. "Private" embraces nongovernmental public granting agencies and private foundations.

The material is viewed from the standpoint of

TABLE 1
TOTAL FUNDS AWARDED BY GOVERNMENT AND PRIVATE SOURCES¹
(1946-51)

	1946-51		1946		1947		1948		1949		1950		1951	
	No. of grants	Amounts	No. of grants	Amounts	No. of grants	Amounts	No. of grants	Amounts	No. of grants	Amounts	No. of grants	Amounts	No. of grants	Amounts
All agencies	12,923	135,044,125	525	4,307,441	997	10,254,340	2065	21,457,747	2803	33,130,112	3317	35,000,370	5216	32,893,609
Government	7216	83,110,671	131	1,871,065	416	5,907,147	1051	12,859,975	1441	19,486,388	2052	21,320,493	2125	21,785,603
Private	5707	51,933,454	394	2,436,376	581	4,447,193	1014	8,597,772	1362	13,663,730	1265	11,680,377	1091	11,108,006



funds available for medical research during the period covered, separated to distinguish amounts awarded by government and by private sources. The first part of this presentation is concerned with the distribution of these amounts by geographical location and fiscal year, an analysis of the size of grants, the amounts received by individual investigators, and the duration of support of research projects. The second part of the presentation is concerned with the distribution of funds by subject field.

The total funds (as recorded with the exchange) awarded for research in the medical and allied fields are considered first. During the six years from 1946

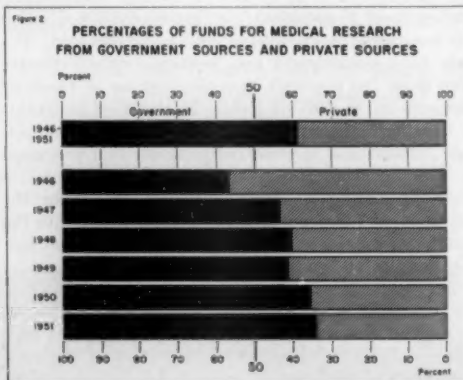
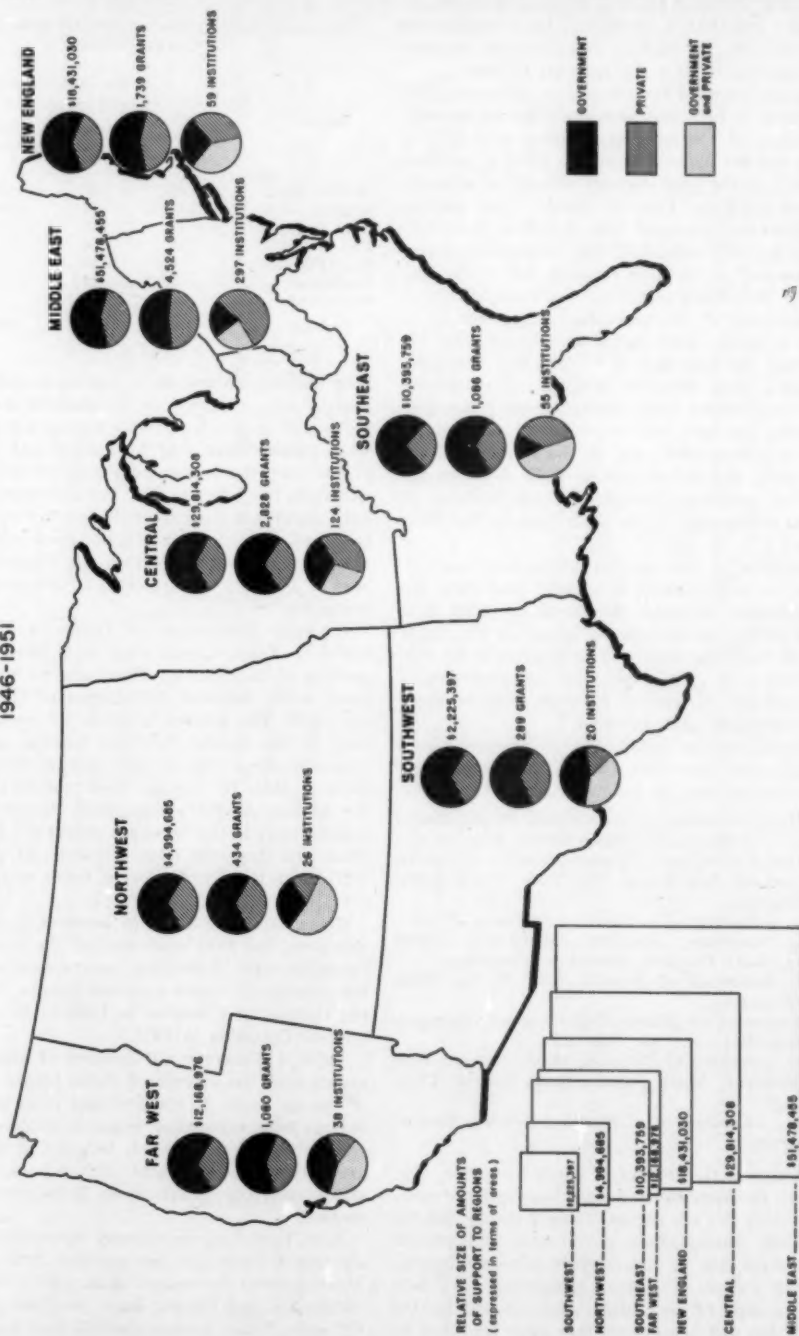


Figure 3

DISTRIBUTION OF FUNDS AND GRANTS BY REGION.
SOURCES OF GRANTS TO INSTITUTIONS WITHIN REGIONS
1946-1951



through 1951, \$135,044,125 was awarded through 12,923 grants; \$83,110,671, or 61.5%, from government and \$51,933,454, or 38.5%, from private sources. Table 1 and Fig. 1 show the amounts by year.

The funds increased from 4 million dollars in 1946 to 33 million in 1949 and have remained at approximately this level. Government support, only 44% in 1946, has steadily increased until, in 1951, it provided nearly 66% of the total support of medical research, as demonstrated in Fig. 2. Funds from private sources, however, increased from 2 million in 1946 to 11 million in 1951, indicating that increasing governmental support of medical research has in no way diminished the efforts of the private foundations.

The disparity of the percentages may not be as great as it seems, since many private agencies are emphasizing the support of "established investigators" rather than research projects. Furthermore, there are indications that, during recent years, private foundations have been responsible for the major support of fellowships and, in the opinion of the authors, little distinction can be made between the support of research through the mechanisms of grants or fellowships. Both contribute to the same objective.

The increase in the support of medical research over this six-year period is clearly less than the figures indicate. Although the funds awarded have increased 800%, the purchasing power of the dollar in research fields has decreased as steadily as its purchasing power in other fields, and interpretation of growing support of medical research must be based upon the increased costs involved.

Fig. 3 presents the distribution of research funds throughout the United States which, for convenience, has been divided into the following six regions:

- New England*, consisting of Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont;
- Middle East*, consisting of Delaware, District of Columbia, Maryland, New Jersey, New York, Pennsylvania, West Virginia;
- Southeast*, consisting of Alabama, Arkansas, Florida, Georgia, Kentucky, Louisiana, Mississippi, North Carolina, South Carolina, Tennessee, Virginia;
- Southwest*, consisting of Arizona, New Mexico, Oklahoma, Texas;
- Central*, consisting of Illinois, Indiana, Iowa, Michigan, Minnesota, Missouri, Ohio, Wisconsin;
- Northwest*, consisting of Colorado, Idaho, Kansas, Montana, Nebraska, North Dakota, South Dakota, Utah, Wyoming;
- Far West*, consisting of California, Nevada, Oregon, Washington.

In addition to the amount of funds by region, Fig. 3 presents the numbers of institutions and the numbers of grants in each region. Table 2 clearly demonstrates that, whereas both government and private agencies cooperate in the support of some institutions, each source of support contributes to a substantial number of institutions not reached by the other. Of the 619 institutions that have benefited by research grants, only 31% received assistance from

TABLE 2
REGIONAL DISTRIBUTION OF INSTITUTIONS BY SOURCE OF GRANTS (1946-51)

Region	No. of institutions			
	Government sources	Private sources	Both sources	Total
Middle East	63	166	68	297
Central	41	47	36	124
New England	17	19	23	59
Far West	16	6	16	38
Southeast	8	20	27	55
Northwest	8	4	14	26
Southwest	9	3	8	20
TOTALS	162	265	192	619

both sources, whereas 43% are supported by private sources only, and 26% by government only. The dispersion of grants by private agencies appears somewhat greater than that by government agencies, as grants from the former were made to 457 institutions and from the latter to 354. Private sources, however, have supported a substantially greater number of institutions only in the Middle East and Southeast regions; in all other regions the disparity in numbers of institutions supported by the two sources is negligible.

Regional distribution of funds by year is illustrated in Table 3, with Figs. 4-4f showing the percentage of distribution. There are no marked differences in the regional distribution of funds over the six years. The greater numbers of research institutions in the Middle East and Central regions quite naturally draw the greater amount of support to these regions. By far the most pertinent measure of the wisdom of the geographical distribution of research funds is the "research potential" developed by Price and Reynolds (*Am. Scientist*, 37, 578 [1949]) with which the distribution of funds compares favorably.

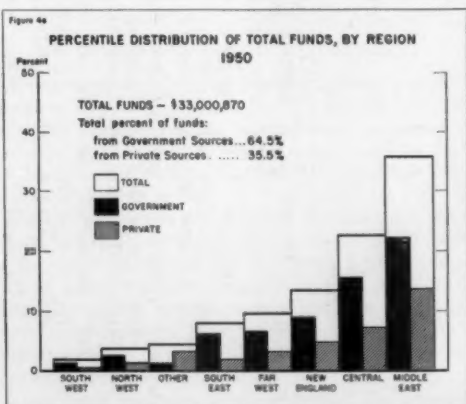
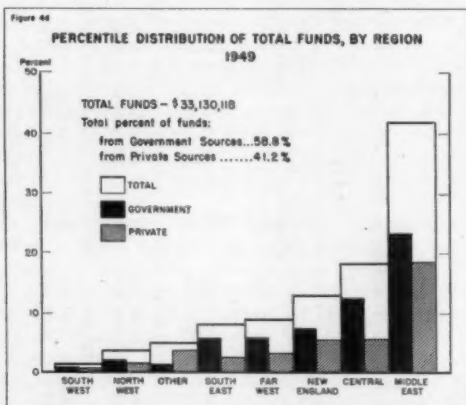
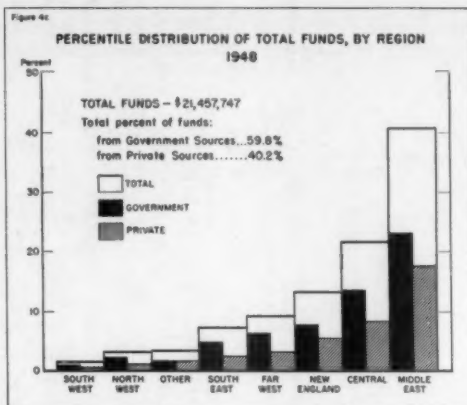
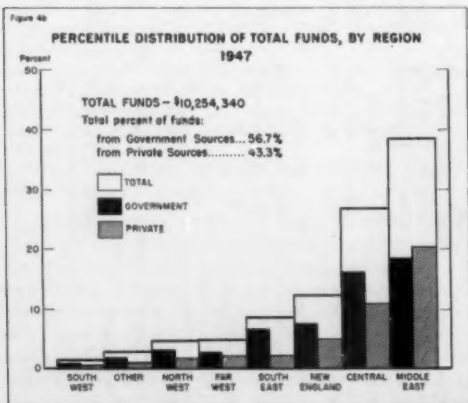
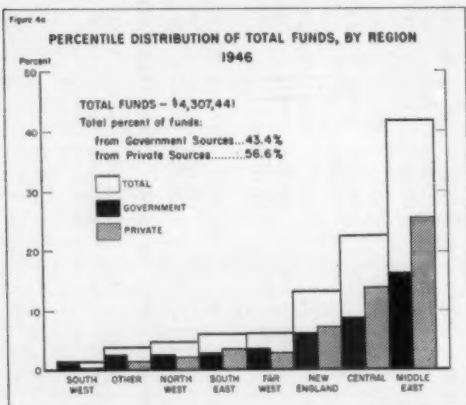
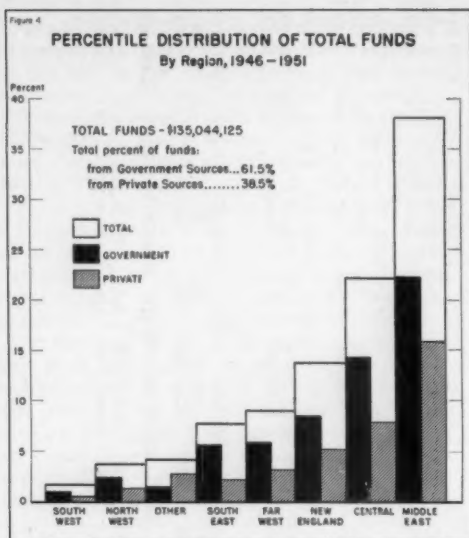
Recognizing the fallacies inherent in any regional grouping, we have also studied the distribution of funds by state. There has been a steady increase in the number of states receiving grants, from 34 and the District of Columbia in 1946 to 48 and the District of Columbia in 1951.

Table 4 illustrates the number of states receiving grants and the sources of these grants during each of the six years. In the first two years private foundations were supporting research in more states than were government agencies, but during the last four years the reverse is true, although the number of states receiving grants from both sources has increased.

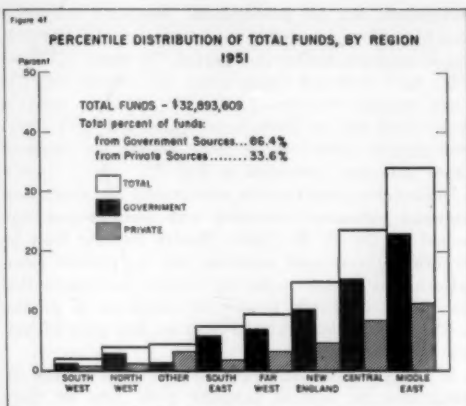
New York has consistently absorbed the greatest amount of funds and has received 20% of the total; Massachusetts is second with 10%; Pennsylvania, California, and Illinois share the third position with 8% each. Table 5 shows that 75% of the total funds have been awarded 11 states.

TABLE 3
REGIONAL DISTRIBUTION OF TOTAL FUNDS

Regions	1946-51			1946			1947			1948			1949			1950			1951		
	No. of grants	Amounts	No. of grants	Amounts	No. of grants	Amounts	No. of grants	Amounts	No. of grants	Amounts	No. of grants	Amounts	No. of grants	Amounts	No. of grants	Amounts	No. of grants	Amounts	No. of grants	Amounts	No. of grants
New England totals	1759	18,431,030	59	569,786	134	1,284,140	273	2,823,862	362	4,337,096	449	4,526,243	402	4,889,903							
Government	987	11,534,939	16	265,317	58	778,424	128	1,651,274	180	2,494,097	285	2,974,714	320	3,374,714							
Private	752	6,896,091	43	304,469	76	505,716	145	1,172,588	182	1,845,983	164	1,552,146	142	1,515,189							
Middle East totals	4524	51,478,455	250	1,808,570	403	3,283,148	759	8,702,702	983	13,925,282	1118	11,803,919	1011	11,264,744							
Government	2386	30,159,504	46	699,966	132	1,891,542	375	4,930,391	475	7,757,013	680	7,316,832	678	7,583,760							
Private	2138	21,318,951	204	1,108,604	271	2,091,606	384	3,772,401	508	6,168,269	438	4,487,087	333	3,680,984							
Southeast totals	1066	10,393,759	46	257,199	95	843,707	163	1,555,795	212	2,615,585	281	2,646,003	259	2,470,470							
Government	721	7,535,341	20	112,085	49	639,991	100	1,048,395	142	1,813,353	203	2,025,915	207	1,895,602							
Private	365	2,858,418	26	145,114	46	208,716	63	507,400	70	802,232	78	620,088	82	574,868							
Southwest totals	289	2,225,397	7	50,961	17	157,157	47	332,522	59	418,044	78	617,085	81	649,628							
Government	184	1,458,522	3	41,891	9	109,895	30	201,915	36	229,914	55	452,996	51	421,911							
Private	105	766,875	4	9,070	8	47,262	17	130,607	23	188,130	23	164,089	30	227,717							
Central totals	2828	29,814,308	110	978,875	280	2,772,896	456	4,656,035	576	6,105,909	757	7,532,965	699	7,767,578							
Government	1874	19,284,507	35	380,775	114	1,647,475	286	2,875,822	382	4,203,174	536	5,149,385	521	5,027,876							
Private	954	10,529,801	75	598,100	116	1,125,421	170	1,780,263	194	1,902,735	221	2,383,580	178	2,739,702							
Northwest totals	434	4,994,685	13	210,124	36	448,631	61	658,591	90	1,145,082	109	1,251,731	125	1,280,526							
Government	280	3,272,947	3	112,095	20	291,298	35	447,715	56	672,226	75	827,581	91	922,032							
Private	154	1,721,738	10	98,029	16	157,333	26	210,876	34	472,856	34	424,150	34	358,494							
Far West totals	1020	12,162,976	26	266,375	54	492,442	159	1,394,828	241	2,981,781	286	3,220,353	314	3,213,192							
Government	662	8,034,756	7	148,486	28	276,467	83	1,334,971	140	1,912,718	185	2,166,670	219	2,195,444							
Private	418	4,134,220	19	117,889	26	215,975	76	659,857	101	1,069,063	101	1,053,683	95	1,017,748							
Other countries totals	943	5,537,515	14	165,551	28	267,219	147	753,272	280	1,601,339	239	1,402,566	235	1,367,568							
Government	122	1,830,155	1	110,450	6	172,055	14	369,492	30	586,877	33	407,017	38	384,264							
Private	821	3,707,360	13	55,101	22	95,164	133	363,780	250	1,214,462	206	995,549	197	983,304							
GRAND TOTALS	12923	135,044,125	595	4,307,441	997	10,254,340	2065	21,457,747	2803	33,130,118	3317	33,000,870	3216	32,893,609							
Government	7216	83,110,671	131	1,871,065	416	5,807,147	1051	12,859,975	1441	19,468,388	2052	21,320,493	2125	21,785,603							
Private	5707	51,933,454	394	2,436,376	581	4,447,193	1014	8,597,772	1362	13,663,730	1265	11,680,377	1091	11,108,006							



Continuing this analysis, we find that 24 states have been awarded a million dollars or more during the period and, in the aggregate, have received 91% of the total funds. All these states, with the exception



of Kansas, first supported in 1947, have been supported in all years. Table 6 shows the 24 states that have received the greatest amount of funds.

Of the remaining states, four (Maine, New Jersey, Iowa, and Florida) have received between one-half and one million dollars; ten states (Alabama, Oregon, Oklahoma, Vermont, Kentucky, Nebraska, South Carolina, Rhode Island, New Mexico, and Arkansas) have received between \$100,000 and \$500,000; the rest (Montana, Wyoming, South Dakota, Arizona, Idaho, Mississippi, Delaware, North Dakota, West Virginia, New Hampshire, and Nevada) have received less than \$100,000. Of this last group, Wyoming alone has received support through all the years concerned. Support for the others was, with a few exceptions, started in 1949, which may be correlated with the wider state distribution of funds from both sources.

With regard to amount of funds awarded, there has been no appreciable change in the relative positions of the several states in any of the years covered by this report; in short, the percentage distribution of funds among the states for each year is essentially comparable to that for the total period.

From our data it is clear that the majority of research grants, whether from government or private agencies, amount to less than \$10,000. This range comprises 68% of all grants, with an even greater number among those of private agencies (77%) than those of government agencies (62%). An additional 20% of all grants fall in the \$10,000-\$20,000 range, this time with a greater number among grants from government (26%) than from private sources (14%). Fig. 5 shows the distribution of grants by size, first for all grants, then for those of government agencies and private agencies independently. Here it is demonstrated that in all instances large grants (\$50,000 and above) represent less than 3% of the total number of grants, and that private sources have awarded slightly more grants in this range than have government sources. Throughout the successive years the figures indicate a diminishing percentage of grants

TABLE 4
NUMBER OF STATES RECEIVING GRANTS

Fiscal year	Number of states*		
	Total supported	Government-supported	Private-supported
1946	35	25	34
1947	37	29	35
1948	40	38	36
1949	43	43	38
1950	47	47	40
1951	49	47	44

* The District of Columbia is counted as a state.

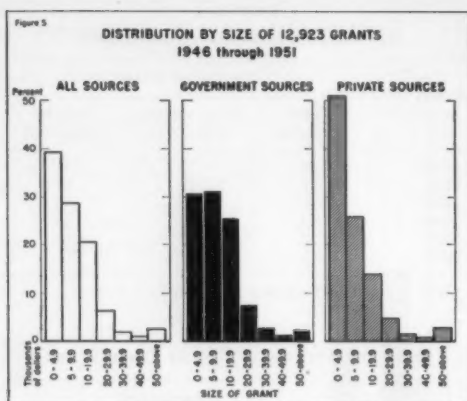
TABLE 5
STATE DISTRIBUTION OF 75% OF TOTAL FUNDS

State	Percentages						
	1946-51	1946	1947	1948	1949	1950	1951
New York	20.24	26.50	20.76	22.10	20.23	19.29	19.02
Massachusetts	9.85	7.62	9.38	9.31	9.12	10.27	10.90
Pennsylvania	7.97	6.12	8.26	7.34	9.84	7.12	7.47
California	7.79	5.06	4.25	8.80	7.94	8.28	8.22
Illinois	7.61	9.03	10.93	7.93	5.62	8.51	7.23
District of Columbia	5.08	4.37	5.05	4.71	4.65	4.71	3.20
Maryland	4.23	3.59	3.82	5.61	3.85	4.13	4.02
Ohio	3.53	2.85	4.68	2.89	3.45	3.76	3.56
Michigan	3.51	2.64	4.05	3.28	2.34	2.94	5.36
Connecticut	2.87	3.96	2.86	2.83	3.14	2.50	2.89
Minnesota	2.78	3.50	3.06	3.09	2.56	2.58	2.89
TOTAL	75.46	75.24	77.10	77.30	75.74	74.09	74.76

TABLE 6
TWENTY-FOUR STATES WITH SUPPORT EXCEEDING 1 MILLION GROUPED IN ORDER OF AMOUNTS AWARDED (1946-51)

Amounts awarded (in millions)			
10 or more	2-10	1.5-2	1-1.5
New York	District of Columbia	Tennessee	Virginia
Massachusetts	Maryland	North Carolina	Colorado
Pennsylvania	Ohio	Utah	Wisconsin
California	Michigan	Texas	Kansas
Illinois	Connecticut		Georgia
	Minnesota		Washington
	Missouri		Indiana
	Louisiana		

in amounts below \$5,000 from both government and private agencies, with a corresponding increase in the \$5,000-\$20,000 range. This shifting in the size of grants is undoubtedly correlated with the rising costs of all elements of research. It became evident as early as 1947 and progressively mounted until, by 1951, 55% (as compared with 37% in 1946) of all grants from all sources appear in the range between \$5,000 and \$20,000. Changes have taken place entirely within the lower categories. No variation has been evidenced in the distribution of numbers of grants in amounts



of \$20,000 and upward during the successive years.

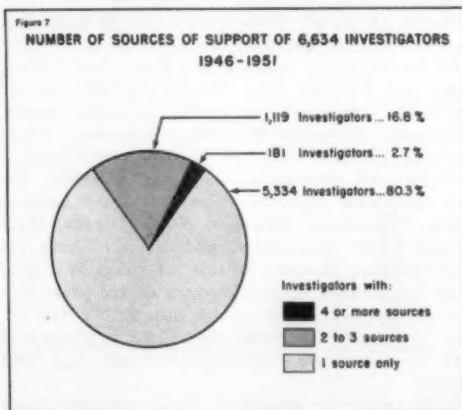
A survey of the duration of support of projects begun in three of the years covered by this report establishes that over 50% of the projects begun in each of these years have received a minimum of three years' support (Fig. 6). Those projects from the year 1946 offer the longest period of survey and show that 42% of all grants begun in that year were supported for five years or more. On the other hand, there has been a substantial increase in the number of grants that have received only one or two years of support. Whether this increase in short-term duration is the result of investigators' requests or of the policies of granting agencies must remain unanswered because the exchange has no knowledge of refusals to continue support. Certainly the short duration of some projects may be attributed to the fact that granting agencies sometimes prefer a trial period to refusal of assistance of first requests, and reflects the increasing tendency of granting agencies to stimulate research wherever potential exists. These facts may indicate the flexibility of programs which can provide opportunity for research to a number of less well-known investigators. Many of these, undoubtedly, are awarded projects of longer duration at later times.

The exchange has been particularly interested in the number of investigators who have received research funds and has listed, not only principal in-

vestigators, but all professional personnel whenever possible. There are 6,634 investigators who have received support during this period. Of these, 5,334, or 80%, have received funds from one source only. A much smaller number—1,119 (17%)—have received funds from two or three sources, and only 181 (3%) have drawn upon four or more sources for support. These data are presented in Fig. 7.

Inasmuch as our records consistently list more professional personnel concerned with each project supported by the U. S. Public Health Service than by the other government agencies and by private foundations, one cannot make the obvious deduction that the spread of funds among investigators is greater on the part of government than on the part of private foundations.

It is significant that even though 20% of the investigators do receive support from two or more sources, the routine procedures of the Medical Sci-



ences Information Exchange ensure that each disbursing agency has full knowledge of the support provided by all others and has adequate opportunity, therefore, to prevent any proposed undesirable duplication of research effort. Further, although we cannot, from our records, make an analysis of the number of sources that an investigator has explored in seeking support, it is considered by all granting agencies and by many investigators as most imperative that an applicant have an opportunity to present his proposal to more than one agency, since in many instances an original and worth-while idea not recognized by or within the scope of one group of reviewing consultants will receive enthusiastic support from another.

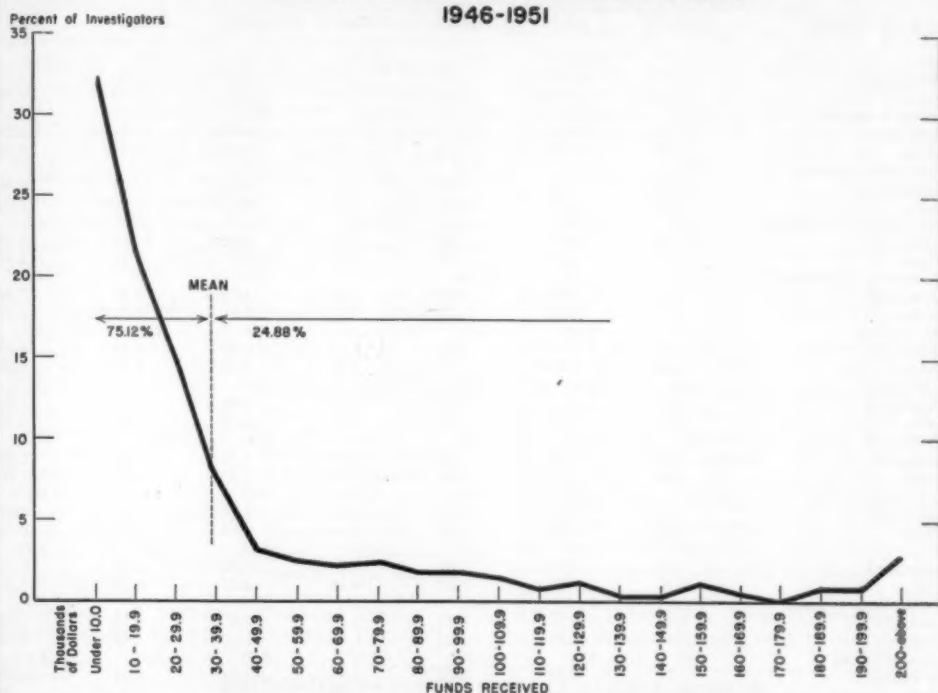
We have been interested in the amount of support received by individual investigators. In discussing these amounts we are concerned only with the cumulative funds over the six-year period, since the funds awarded a man during a single year are meaningless. The data as presented in Fig. 8 show that by far the greatest number of investigators (80%) have been

Figure 8
DURATION OF SUPPORT OF RESEARCH GRANTS

FIRST YEAR OF SUPPORT	PERCENTAGE OF GRANTS SUPPORTED					
	1 YEAR	2 YEARS	3 YEARS	4 YEARS	5 YEARS	6 YEARS
1946 - TOTAL	7	10	21	20	19	23
Government	9	12	10	21	22	26
Private	6	9	30	18	16	21
1948 - TOTAL	20	21	19	40		
Government	22	24	20	34		
Private	17	17	18	48		
1949 - TOTAL	22	24	54			
Government	19	29	52			
Private	26	17	57			

Figure 8

AMOUNT OF SUPPORT TO INVESTIGATORS 1946-1951



individually granted less than \$50,000 and, indeed, 69% have received less than \$30,000. Investigators who have received research support in amounts of more than \$200,000 dollars, over the six-year period, constitute less than 3% of all investigators listed and are those men who are heading large research teams or whose work requires the purchase of expensive apparatus. The mean amount was \$37,000, the median \$16,000, and 75% of all investigators received less than, and only 25% more than, the mean. Certainly, figures such as these indicate that the distribution of research funds among investigators is extremely broad.

An analysis of the distribution of these grants by subject should be preceded by a brief statement of the content of the exchange and the development of its method of indexing. In spite of its name, no rigid definition of medical research has directed the accumulation of subject material. Rather, the content has grown in accordance with the research grant and contract programs of those government agencies supporting the Medical Sciences Information Exchange and which cooperated in the activities of its predecessor, the Office of Exchange of Information, Public Health Service. Construction, teaching aid, and disease control programs of government agencies have never been a part of the exchange.

In developing cooperation with private foundations, the exchange has selected those foundations and programs that are allied to the interests of the supporting agencies, and has, as in the instance of government, excluded rehabilitation and control activities not concerned with investigative research. This flexibility in approach has enabled expansion with the growing interests of the cooperating agencies, permitting the inclusion of research in all fields ancillary to medicine. Consequently, human resources and basic studies in the social sciences have a place in the material. Many people will be gratified to find interdisciplinary relationships taking an increasingly important part in medical research.

The development of a subject index for the day-by-day purposes of the exchange presented particular problems. An exhaustive exploration of existing classifications of medical research resulted in the decision reached many times before, that the only adequate method is one planned to meet specific needs. The index was developed to serve a twofold purpose—to point the way to logical grouping of related research and to furnish a guide to specific detail. In meeting its objectives, it, like the subject matter, grew in accordance with the expansion of the programs of the cooperating agencies. This report will not deal with the detail of the index, but

TABLE 7
PERCENTILE DISTRIBUTION OF FUNDS BY SUBJECT FIELD (Single Category)

Subject category	1946-51	1946	1947	1948	1949	1950	1951
Cancer	19.54*	14.35*	8.24	23.40	19.59	20.37	20.34
Government	14.75†	19.08†	5.72	14.74	15.74	15.70	14.98
Private	27.21‡	10.71‡	11.52	36.36	25.08	28.89	30.87
Infectious Diseases	17.68	22.18	28.58	18.03	16.15	15.65	17.06
Government	17.23	32.02	38.12	21.53	16.09	13.48	12.55
Private	18.41	14.62	16.13	12.78	16.24	19.61	25.91
Cardiovascular System	8.76	6.27	8.98	6.14	6.20	10.50	11.57
Government	10.90	5.53	8.86	7.69	6.52	13.77	14.90
Private	5.34	6.84	9.14	3.83	5.73	4.52	5.04
General Medical Problems	7.34	10.52	8.66	6.43	6.70	7.76	7.35
Government	10.04	19.06	11.91	8.88	9.55	10.29	9.63
Private	3.04	3.97	4.42	2.76	2.65	3.14	2.87
Metabolism & Nutrition	5.69	9.21	6.24	6.01	5.24	5.50	5.49
Government	5.07	4.97	3.56	4.87	4.78	5.40	5.55
Private	6.67	12.46	9.74	7.71	5.90	5.68	5.37
Mental Health	4.29	0.65	1.60	4.70	4.65	4.05	5.20
Government	5.38	—	1.50	6.18	6.10	4.73	6.38
Private	2.55	1.15	1.74	2.49	2.58	2.81	2.89
Basic Studies	3.53	0.90	1.44	2.11	4.76	4.16	3.59
Government	3.57	—	1.18	1.62	4.86	4.23	3.87
Private	3.46	1.60	1.77	2.84	4.61	4.05	3.02
Public Health	3.29	3.42	4.33	4.23	2.94	3.47	2.50
Government	3.69	1.23	4.57	4.74	3.57	3.98	2.86
Private	2.64	5.10	4.01	3.47	2.03	2.52	1.80
Nervous System	2.85	2.28	2.61	2.88	3.17	2.62	2.91
Government	3.15	2.43	3.20	3.50	3.46	2.60	3.24
Private	2.39	2.16	1.84	1.96	2.75	2.65	2.26
Blood	2.62	2.02	3.50	2.04	1.68	2.00	4.36
Government	3.96	4.01	5.94	3.28	2.64	2.79	6.15
Private	0.47	0.50	0.33	0.19	0.31	0.56	0.85
Musculoskeletal System	2.42	3.09	1.63	2.79	2.12	2.35	2.38
Government	2.94	5.70	1.26	3.58	2.47	3.13	3.02
Private	1.50	1.09	2.12	1.62	1.62	1.49	1.13
Endocrine System	2.26	1.05	0.88	1.92	2.08	2.47	3.06
Government	2.76	0.56	0.62	2.09	2.61	2.91	3.90
Private	1.47	1.43	1.21	1.68	1.32	1.65	1.39
Problems of Children	2.04	1.85	1.57	1.86	2.01	2.24	2.15
Government	1.60	0.41	0.57	1.49	1.52	1.71	2.06
Private	2.72	2.96	2.88	2.42	2.71	3.21	2.33
Digestive System	1.43	0.06	0.54	1.58	1.61	1.70	1.35
Government	2.29	—	0.93	2.63	2.72	2.59	1.99
Private	0.05	0.10	0.02	—	0.04	0.08	0.09
Human Resources	1.23	1.13	1.93	1.63	0.97	1.48	0.80
Government	1.79	2.60	3.18	2.61	1.54	1.95	0.93
Private	0.35	—	0.30	0.16	0.17	0.62	0.54
Sensory Organs	1.06	0.70	1.06	0.99	0.88	1.32	1.10
Government	1.51	0.81	1.35	1.36	1.35	1.93	1.44
Private	0.35	0.62	0.67	0.43	0.21	0.22	0.42
Urogenital System	0.88	0.06	0.70	0.63	0.62	1.03	1.32
Government	1.12	—	0.30	0.72	0.83	1.35	1.70
Private	0.50	0.10	1.23	0.50	0.32	0.45	0.57
Ageing	0.83	0.57	0.53	0.99	0.72	0.94	0.86
Government	0.91	—	0.16	1.08	0.84	1.09	0.97
Private	0.71	1.01	1.02	0.84	0.55	0.68	0.65
Dental Problems	0.81	1.14	0.75	0.71	0.68	0.89	0.89
Government	1.17	1.01	0.97	1.10	1.04	1.23	1.31
Private	0.23	1.23	0.46	0.12	0.17	0.26	0.07
Respiratory System	0.56	—	1.16	0.37	0.43	0.53	0.74
Government	0.79	—	2.05	0.57	0.63	0.68	0.91
Private	0.19	—	—	0.08	0.13	0.25	0.39
Integumentary System	0.49	0.25	0.20	0.22	0.42	1.04	0.30
Government	0.77	0.58	0.30	0.33	0.70	1.58	0.45
Private	0.04	—	0.06	0.06	0.03	0.06	0.03
Occupational Diseases	0.19	—	0.48	0.27	0.13	0.21	0.11
Government	0.26	—	0.84	0.45	0.20	0.22	0.10
Private	0.07	—	—	—	0.03	0.18	0.14
Other	10.21	18.29	14.39	10.06	16.25	7.52	4.56
Government	4.34	—	2.91	4.96	10.24	2.65	1.09
Private	19.61	32.34	29.37	17.68	24.82	16.41	11.36

* Percentage of total funds. † Percentage of government funds. ‡ Percentage of private funds.

utilizes the broad research relationships developed through it.

The subject matter is presented under two systems, the single category method and the multiple category method. Under the former, each grant is placed in only one category to provide, for the purposes of this paper, a division of research funds among subject fields. Under the multiple system, which is based upon the index developed by the exchange, each grant is placed in as many major categories as the content of the project warrants but, it must be emphasized, is included only once within any individual major category. Listed below are the topics used in each of these systems.

Single Subject Categories

Ageing
Basic Studies
Blood
Cancer
Cardiovascular System
Dental Problems
Digestive System
Endocrine System
General Medical Problems
Human Resources
Infectious Diseases
Integumentary System
Mental Health
Metabolism and Nutrition
Musculoskeletal System

Multiple Subject Categories

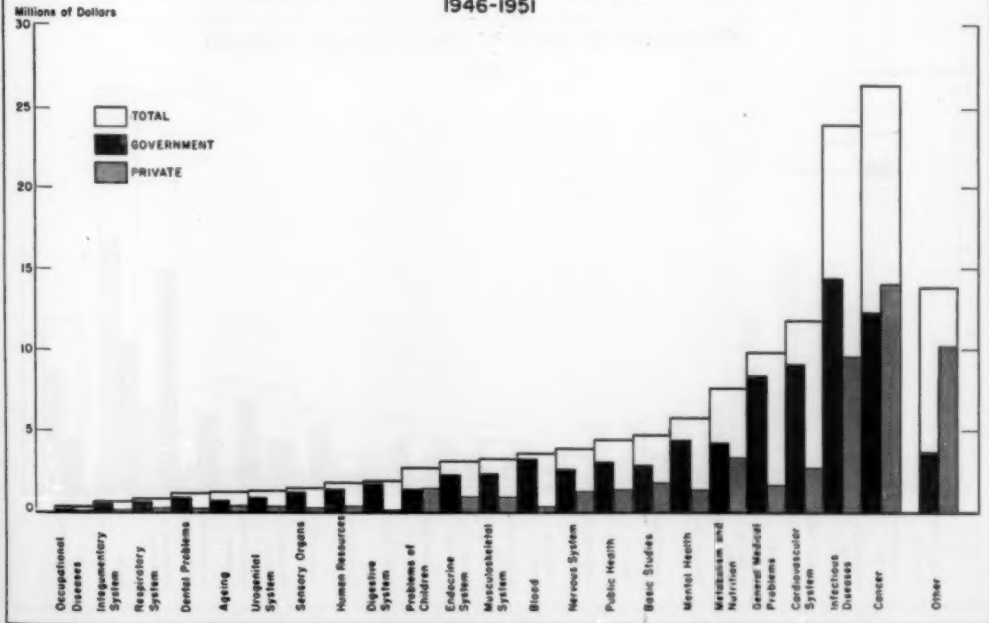
Ageing
Allergy and Anaphylaxis
Anesthesia and Analgesia
Blood
Cancer
Cardiovascular System
Deficiency Diseases and Nutrition
Dental Research
Digestive System
Ecology and Environment
Emotional and Psychiatric States
Endocrine System
Infectious Diseases

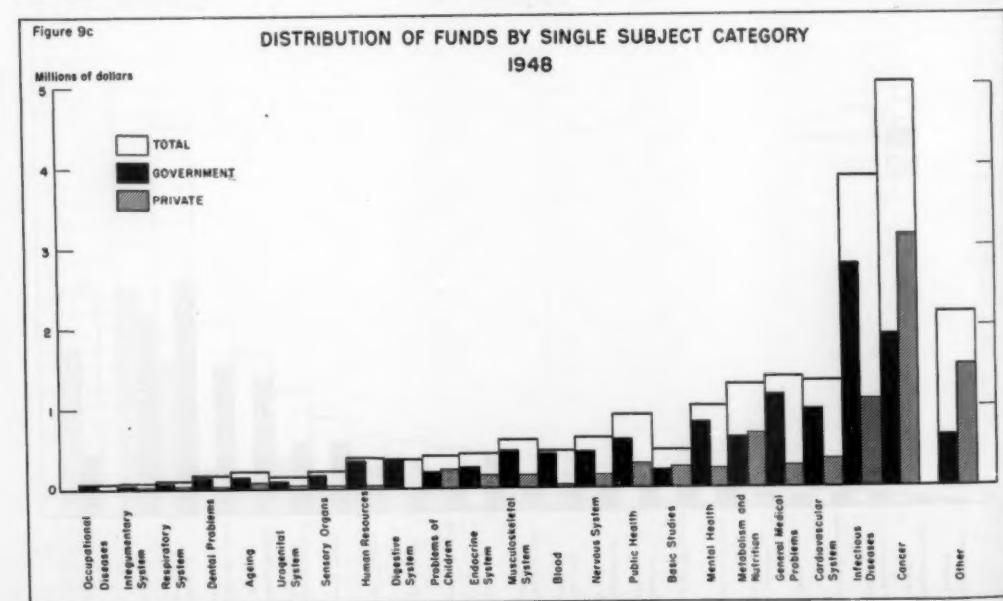
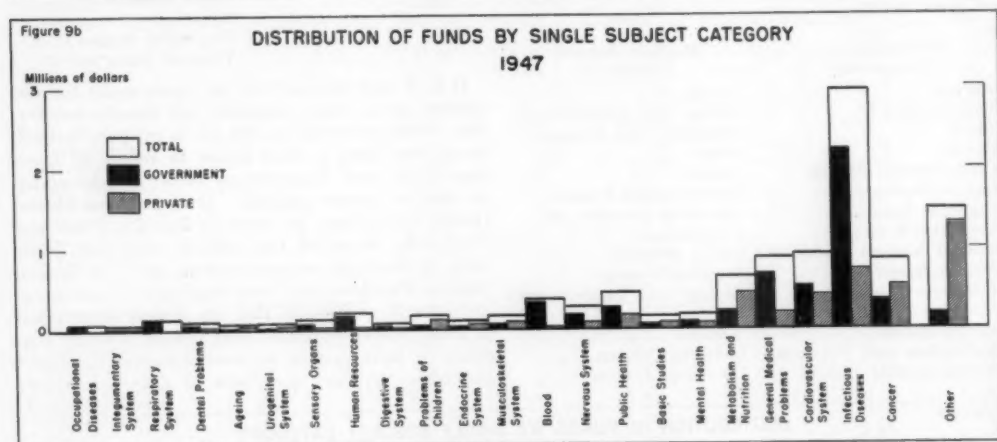
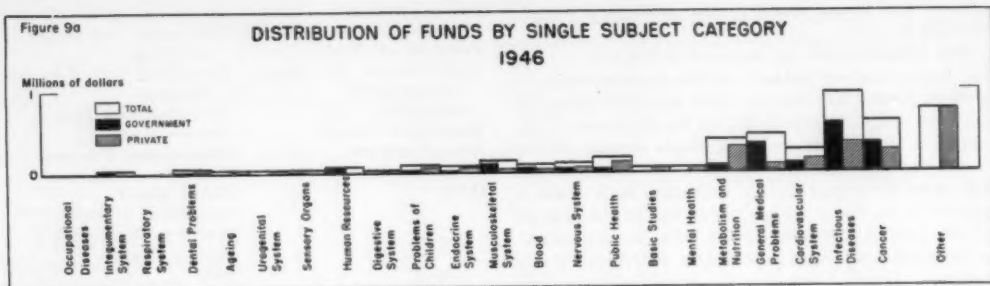
Nervous System
Occupational Diseases
Problems of Children
Public Health (including Environmental Sanitation)
Respiratory System
Sensory Organs
Urogenital System
Other

Injury and Shock
Intoxication and Drug Addiction
Metabolism and Metabolic Diseases
Musculoskeletal System
Nervous System
Occupational Diseases
Problems of Children
Public Health
Respiratory System
Sanitary Engineering
Sensory Organs
Skin
Social Sciences
Stress
Urogenital System
Venereal Diseases

It is at once obvious that the topics under the two systems are in many instances not directly comparable. It was necessary, in the single category method, to employ more general topics to reduce in small measure, at least, the arbitrary factor of determining the field of major emphasis: thus the term Mental Health rather than the more limited Emotional and Psychiatric States of the multiple categories. Similarly, in the single category system, the term General Medical Problems has been employed to provide a place for those projects that are clinical in part and in which major emphasis went beyond a single condition or body system. In most instances the topics are self-explanatory and need no definition. Under

Figure 9
DISTRIBUTION OF FUNDS BY SINGLE SUBJECT CATEGORY
1946-1951





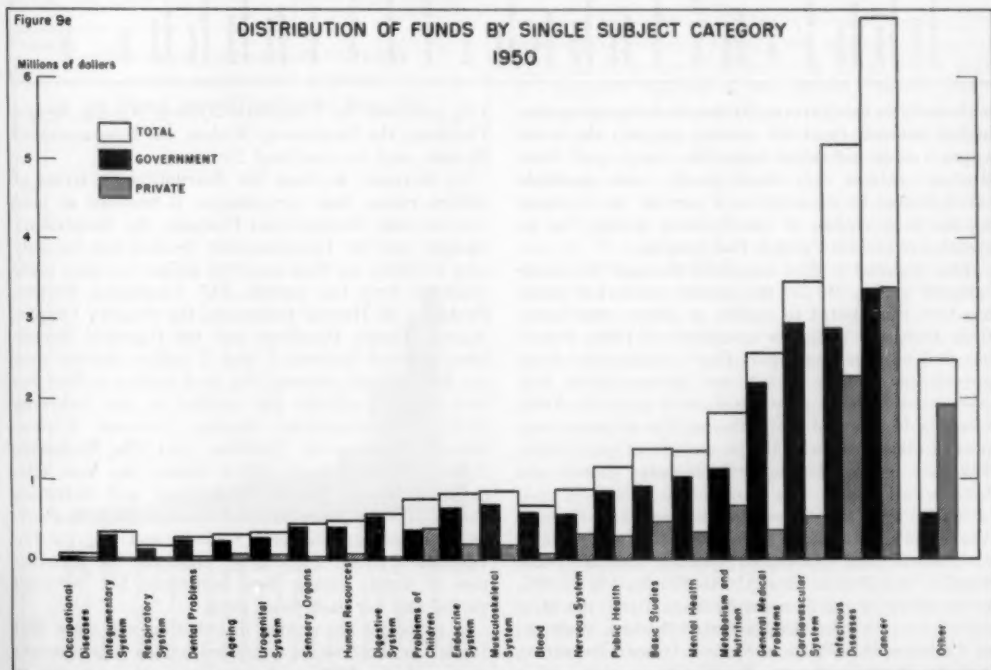
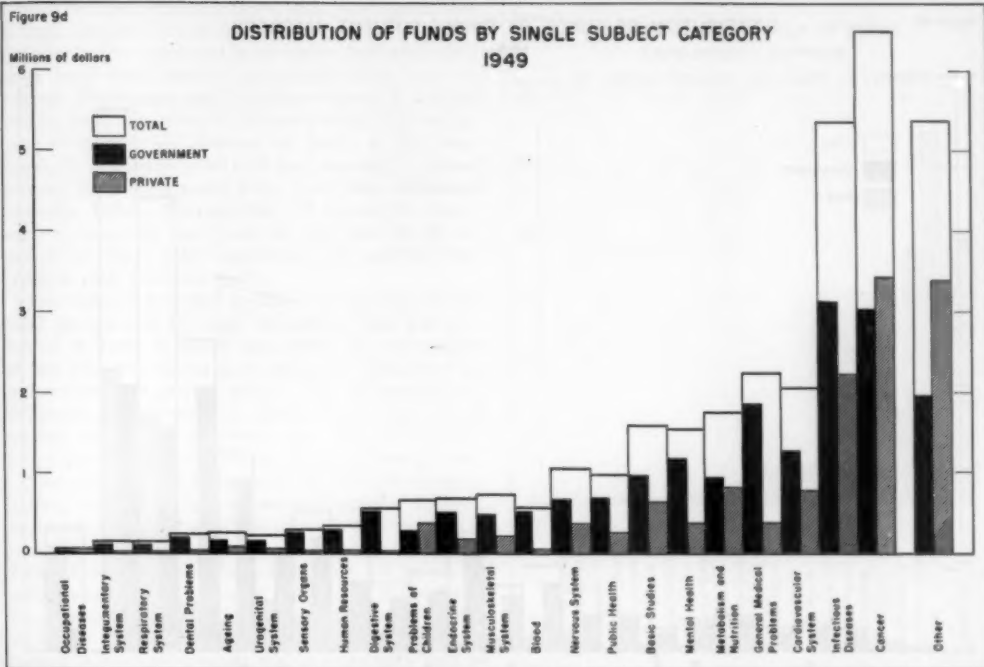
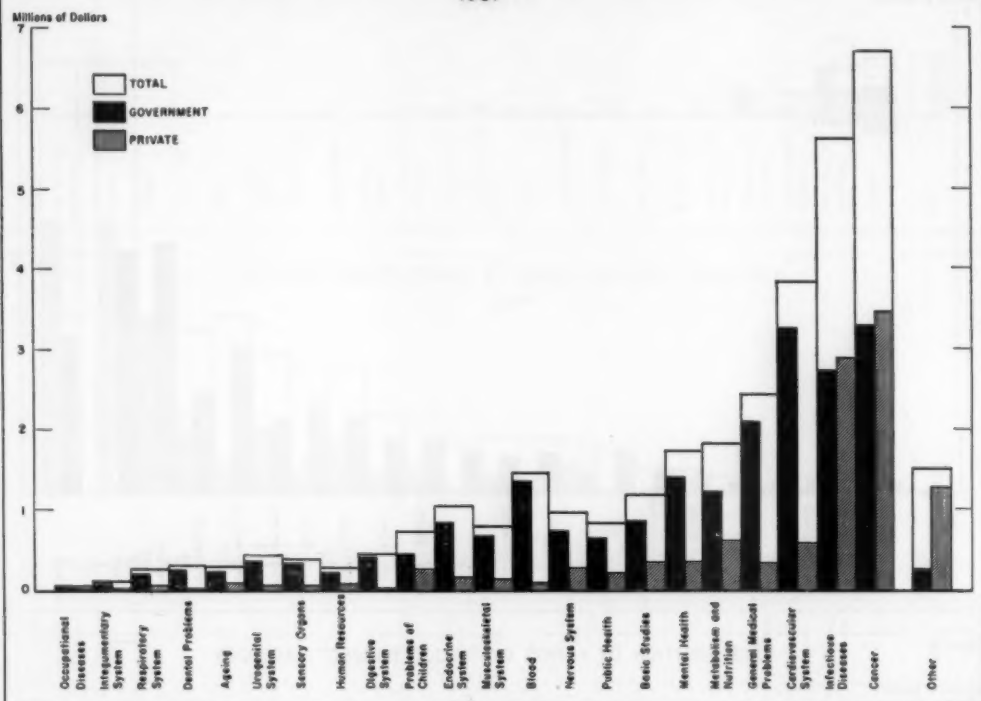


Figure 9f

DISTRIBUTION OF FUNDS BY SINGLE SUBJECT CATEGORY
1951

both methods the Nervous System excludes nonneurological problems and the sensory organs; the latter appears as an individual topic. The category of Basic Studies contains only those purely basic problems which cannot be regarded as a part of more concise topics; basic studies of the digestive system, for instance, are included within that system.

This material is first examined through the single category system. By far the greatest amount of funds has been contributed to studies of Cancer and Infectious Diseases. With the exception of 1946, Cancer has derived greater support from private than from government sources. Infectious Diseases were supported more liberally by government agencies. Table 7 may be interpreted as illustrating five ranges of support in accordance with the percentage of total funds. The first range, 18% to 20%, includes Cancer and Infectious Diseases; the second, 7% to 9%, is comprised of the Cardiovascular System and General Medical Problems; the third, 3% to 6%, contains Metabolism and Nutrition, Mental Health, Basic Studies, and Public Health; the fourth, 1% to 3%, is composed of the Nervous System, Blood, the Musculoskeletal System, the Endocrine System, Problems of Children, the Digestive System, Human Resources, and the Sensory Organs. The final range, less than

1%, embraces the Urogenital System, Ageing, Dental Problems, the Respiratory System, the Integumentary System, and Occupational Diseases.

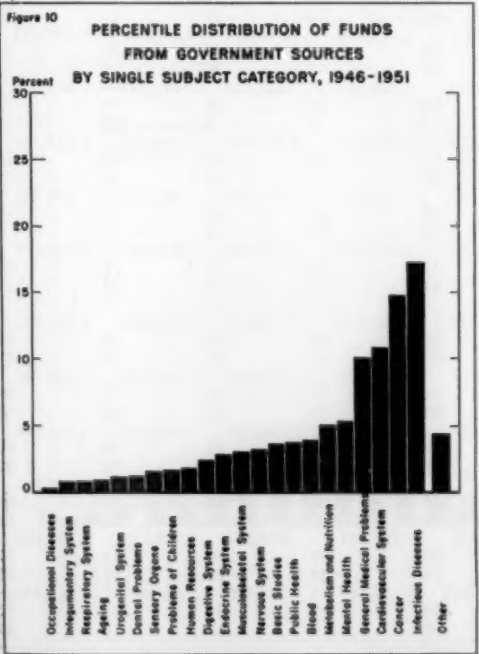
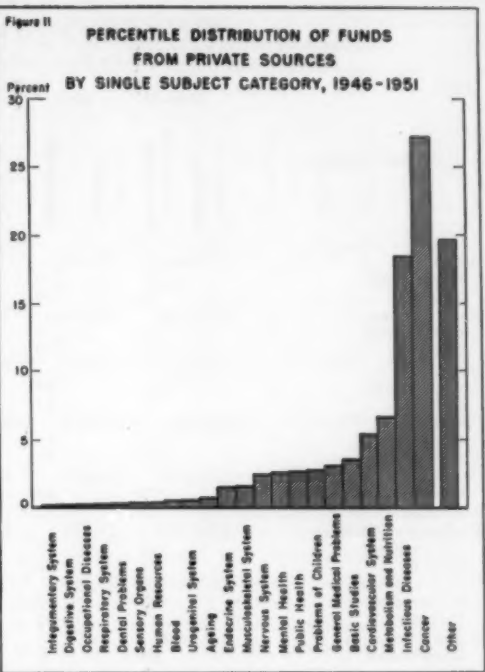
If, however, we view the distribution in terms of dollars rather than percentages, it becomes at once obvious that Occupational Diseases, the Respiratory System, and the Integumentary System are the only ones to which less than a million dollars has been made available over the period. The Urogenital System, Problems of Human Resources, the Sensory Organs, Ageing, Dental Problems, and the Digestive System have received between 1 and 2 million dollars over the total period, whereas $2\frac{1}{2}$ to 4 million dollars has been made available for studies in the following fields: Musculoskeletal System, Nervous System, Blood, Problems of Children, and the Endocrine System. More than 4 million dollars has been allocated to Mental Health, Metabolism and Nutrition, Public Health, Basic Studies, General Medical Problems, Infectious Diseases, Cancer, and the Cardiovascular System. Figs. 9-9f illustrate the distribution of funds among these categories for the total period and for each fiscal year.

A glance at the annual distribution will show that funds for most topics increased as the total amount increased. In 1948 a sharp rise in the support of

cancer research is shown from both government and private sources. Increases in funds for the Cardiovascular System occurred in all years. Infectious Diseases have been liberally supported throughout the period. Metabolism and Nutrition shows a marked rise in 1948, but when it is remembered that in this year there was an increase of 100% in the total funds, it can scarcely be said that increased support for any field could result from more than additional available funds. The selection of topics for single subject categories was made on the basis of the research involved; fields which are not included have received little or no support.

The amounts awarded the single categories for the total period and for each successive year are presented in Table 8, which also shows the percentages of the amounts within each category contributed by government and private sources. Fig. 10 presents the percentile distribution of funds from government among the single categories, and Fig. 11 presents information concerning funds from private sources.

The subject analysis through the multiple category system, which now follows, is based upon a different approach to the data. At the expense of repetition it must be restated that under this system funds are included in more than one major topic, but only once within each. Funds allocated for cancer of the digestive system, by way of illustration, are included with those for the digestive system as well as those for cancer. Accordingly, funds within a category may be added, but those attributed to two or more categories



may not be combined. In the opinion of the authors, this system presents a more real picture of support of fields of research by including all problems with a reasonable relation to the subject, thereby eliminating many of the arbitrary decisions inherent in the single category system. This material also differs from the single category analysis in that it deals with selected topics and does not include the total body of the index. The topics chosen are believed to be those of greatest interest and most closely related to the topics evolved through the single category system. The material deals in the main with major categories and touches only slightly upon the divisions within them.

The multiple categories have also been grouped by levels of support, in this instance, to show progression of support through the six-year period. Table 9 presents not only the levels of support, but the order of magnitude of support of all topics which received, during any one year, \$400,000 or more. It was not until 1948, when Cancer received a little more than 5 million dollars, that any area of research reached this level. In successive years, first, Infectious Diseases, second, Cardiovascular Research, and, last, Metabolic Studies were financed in amounts above 5 million dollars. Venereal Diseases is the only group relatively well supported in 1946 and 1947 which received under \$400,000 in 1951.

There is no need to trace further the amount of support for each subject category through the suc-

TABLE 8
DISTRIBUTION OF FUNDS BY SINGLE SUBJECT CATEGORY
(Percentage of Funds within Each Category from Government and Private Sources)

Subject category	1946-51		1946		1947		1948		1949		1950		1951	
	Amounts	Percentage	Amounts	Percentage	Amounts	Percentage	Amounts	Percentage	Amounts	Percentage	Amounts	Percentage	Amounts	Percentage
Ageing	1,125,297		24,498		54,458		211,581		240,060		311,640		283,075	
Government		67		0		17		66		68		74		75
Private		33		100		83		34		32		26		25
Basic Studies	4,769,150		38,900		147,445		452,612		1,575,936		1,374,590		1,179,667	
Government		62		0		47		46		60		66		72
Private		38		100		53		54		40		34		28
Blood	3,534,811		87,138		359,216		438,301		555,799		660,476		1,433,891	
Government		93		86		96		96		92		90		93
Private		7		14		4		4		8		10		7
Cancer	26,389,761		617,918		844,654		5,021,503		6,492,101		6,722,145		6,691,440	
Government		46		58		39		38		47		50		49
Private		54		42		61		62		53		50		51
Cardiovascular System	11,332,433		270,237		921,003		1,318,164		2,052,470		3,463,494		3,807,065	
Government		77		38		56		75		62		85		85
Private		23		62		44		25		38		15		15
Problems of Children	2,752,629		79,882		161,236		399,763		665,633		739,057		707,058	
Government		49		10		20		48		44		49		63
Private		51		90		80		52		56		51		37
Dental Problems	1,090,653		48,900		76,862		151,786		225,367		293,512		294,226	
Government		89		39		73		93		90		90		97
Private		11		61		27		7		10		10		3
Digestive System	1,933,596		2,500		54,926		338,405		533,598		561,281		442,886	
Government		99		0		98		100		99		98		98
Private		1		100		2		0		1		2		2
Endocrine System	3,056,095		45,400		90,131		412,840		688,203		813,927		1,005,594	
Government		75		23		40		65		74		76		85
Private		25		77		60		35		26		24		15
General Medical Problems	9,919,701		453,320		888,031		1,379,032		2,221,424		2,560,243		2,417,651	
Government		84		79		78		83		84		86		87
Private		16		21		22		17		16		14		13
Human Resources	1,668,638		48,576		197,893		348,334		322,913		488,088		262,329	
Government		89		100		93		96		93		85		77
Private		11		0		7		4		7		15		23
Infectious Diseases	23,881,831		955,367		2,930,872		3,863,708		5,350,989		5,163,800		5,612,095	
Government		60		63		75		72		59		56		49
Private		40		37		25		28		41		44		51
Integumentary System	663,948		10,798		20,198		48,137		140,053		344,479		100,283	
Government		97		100		88		90		97		98		97
Private		3		0		12		10		3		2		3
Mental Health	5,788,200		27,978		164,426		1,008,899		1,539,352		1,336,668		1,710,877	
Government		77		0		53		79		77		75		81
Private		23		100		47		21		23		25		19
Metabolism and Nutrition	7,681,603		396,582		639,796		1,289,448		1,735,709		1,814,217		1,805,251	
Government		55		23		32		49		54		63		67
Private		45		77		68		51		46		37		33
Musculoskeletal System	3,226,545		133,227		167,574		599,483		701,593		840,788		783,380	
Government		76		80		44		77		68		79		84
Private		24		20		56		23		32		21		16
Nervous System	3,855,634		98,295		267,593		618,307		1,048,966		864,632		957,391	
Government		68		46		69		73		64		64		74
Private		32		54		31		27		36		36		26
Occupational Diseases	255,537		—		48,800		57,546		42,890		68,954		37,347	
Government		84		—		100		100		91		60		60
Private		16		—		0		0		9		31		40
Public Health	4,440,198		147,356		444,053		908,134		972,924		1,143,890		823,839	
Government		69		16		60		67		72		74		76
Private		31		84		40		33		28		26		24
Respiratory System	756,966		—		119,060		30,360		141,199		174,431		241,856	
Government		87		—		100		91		87		83		82
Private		13		—		0		9		13		17		18

TABLE 8—(Continued)
DISTRIBUTION OF FUNDS BY SINGLE SUBJECT CATEGORY
(Percentage of Funds within Each Category from Government and Private Sources)

Subject category	1946-51		1946		1947		1948		1949		1950		1951	
	Amounts	Percentage	Amounts	Percentage	Amounts	Percentage	Amounts	Percentage	Amounts	Percentage	Amounts	Percentage	Amounts	Percentage
Sensory Organs	1,438,788		30,150		108,253		211,857		291,819		436,278		360,431	
Government	87		50		72		82		90		94		87	
Private	13		50		25		18		10		6		13	
Urogenital System	1,191,170		2,520		72,200		135,923		205,998		340,215		434,314	
Government	78		0		24		68		79		85		85	
Private	22		100		76		32		21		15		15	
All Other	13,790,893		787,904		1,475,655		2,158,124		5,385,142		2,483,405		1,500,663	
Government	26		0		11		30		37		23		16	
Private	74		100		89		70		63		77		84	
GRAND TOTALS	135,044,125		4,307,441		10,254,340		21,457,747		33,130,118		33,000,870		32,893,609	
Government	62		43		57		60		59		65		66	
Private	38		57		43		40		41		35		34	

cessive years, but whereas only two areas of research were supported in the amount of a million or more in 1946 or 1947, there were twelve areas supported in this amount in 1948, fifteen in 1949 and 1950, and sixteen in 1951.

Although the greatest funds have consistently been assigned to studies concerned with Cancer, Infectious

Diseases, and the Cardiovascular System, with each passing year other types of research gain increased support, and there is a constantly widening spread of funds among the various areas of medical investigation. Our experience demonstrates conclusively that it is the rare project whose significance is confined to a single field of research; consequently studies in

Figure 12

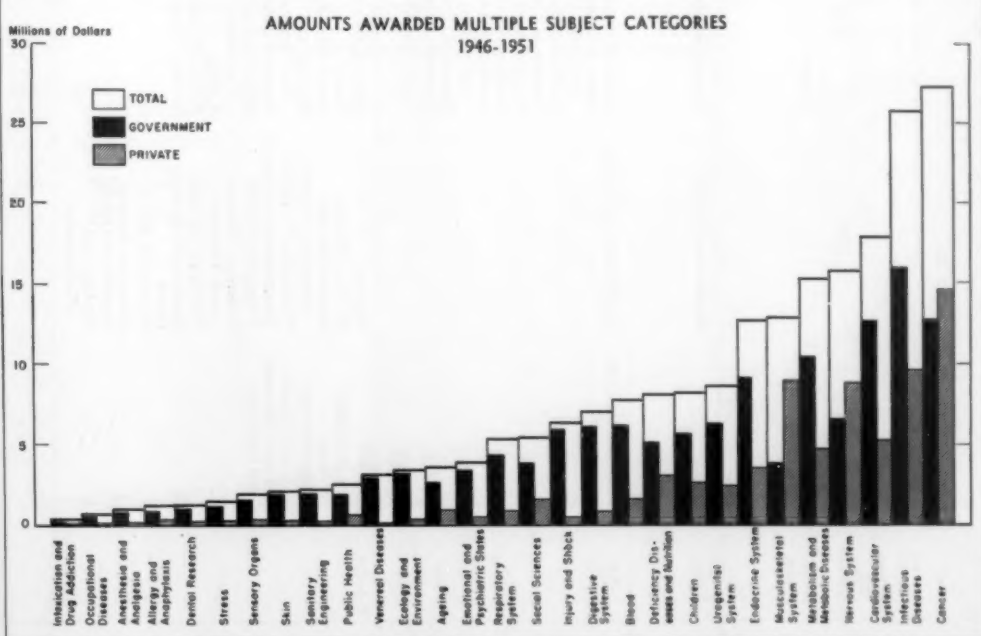


TABLE 9
ORDER OF MAGNITUDE OF SUPPORT OF SELECTED MAJOR MULTIPLE CATEGORIES

Dollars (in millions)	Fiscal years					
	1946	1947	1948	1949	1950	1951
5 and above			Cancer	Cancer Infectious Diseases	Cancer Infectious Diseases Cardiovascular System	Cancer Infectious Diseases Cardiovascular System Metabolism and Metabolic Diseases
3-4.9		Infectious Diseases	Infectious Diseases	Nervous System Cardiovascular System	Metabolism and Metabolic Diseases Nervous System Endocrine System	Nervous System Endocrine System Musculoskeletal System Blood
1-2.9	Infectious Diseases	Cardiovascular System	Nervous System Metabolism and Metabolic Diseases Cardiovascular System Endocrine System Musculoskeletal System Problems of Children Deficiency Diseases and Nutrition Urogenital System Digestive System Injury and Shock	Metabolism and Metabolic Diseases Musculoskeletal System Endocrine System Urogenital System Deficiency Diseases and Nutrition Problems of Children Digestive System Blood Injury and Shock Respiratory System Social Sciences	Musculoskeletal System Urogenital System Deficiency Diseases and Nutrition Problems of Children Digestive System Blood Injury and Shock Social Sciences Respiratory System	Urogenital System Deficiency Diseases and Nutrition Problems of Children Digestive System Injury and Shock Respiratory System Social Sciences Emotional and Psychiatric States
0.4-0.9	Cancer Musculoskeletal System Nervous System Venereal Diseases Deficiency Diseases and Nutrition	Cancer Nervous System Metabolism and Problems of Children Musculoskeletal System Urogenital System Deficiency Diseases and Nutrition Venereal Diseases Respiratory System Blood Injury and Shock Endocrine System Digestive System Ecology and Environment	Social Sciences Blood Respiratory System Ecology and Environment Venereal Diseases Emotional and Psychiatric States Ageing Public Health Sanitary Engineering	Emotional and Psychiatric States Ageing Ecology and Environment Venereal Diseases Sanitary Engineering	Ageing Emotional and Psychiatric States Integumentary System Public Health Ecology and Environment Sanitary Engineering Sensory Organs Venereal Diseases	Ageing Ecology and Environment Stress Psychiatric System Public Health Sensory Organs Sanitary Engineering Allergy and Anaphylaxis

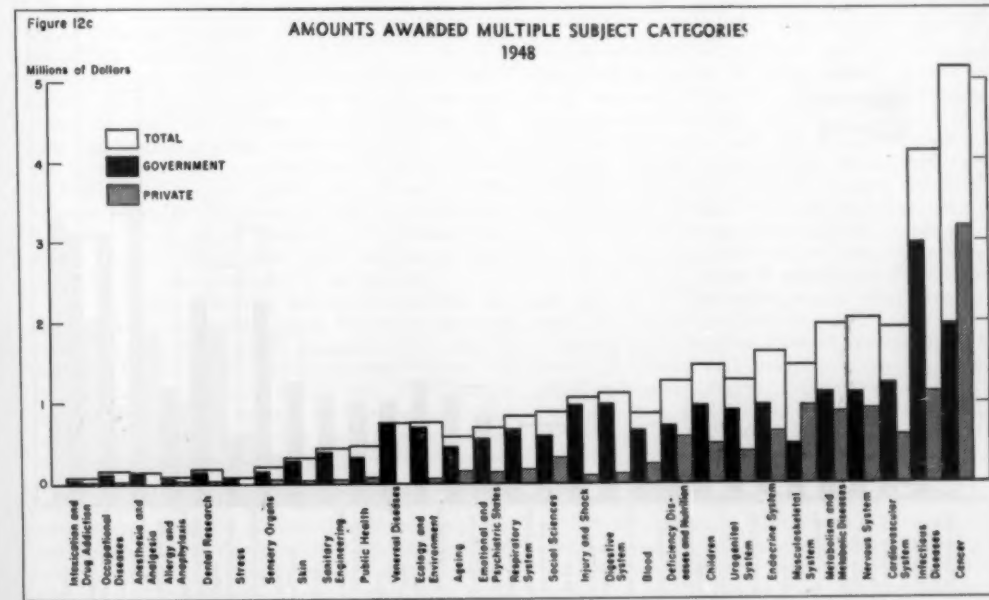
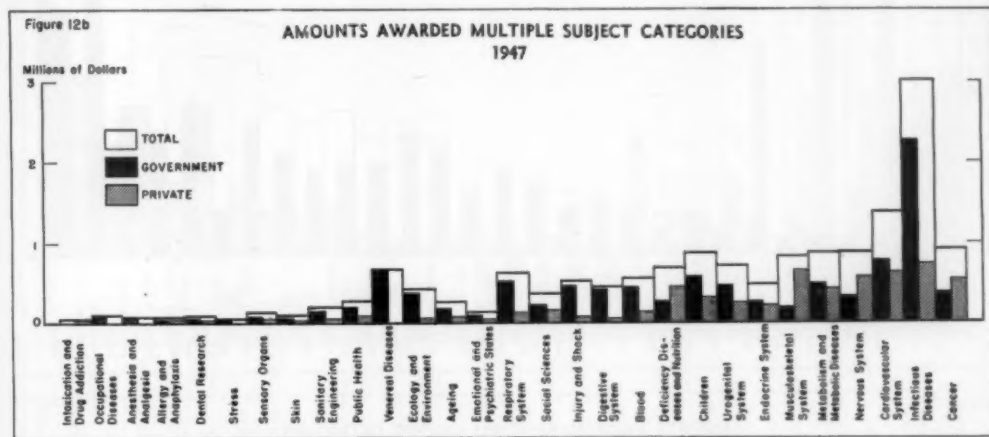
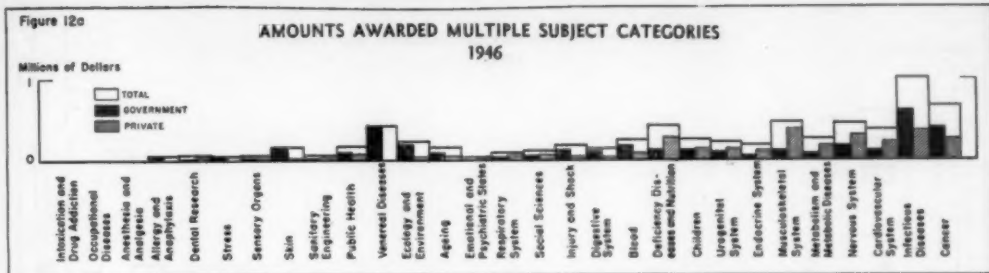


Figure 12d

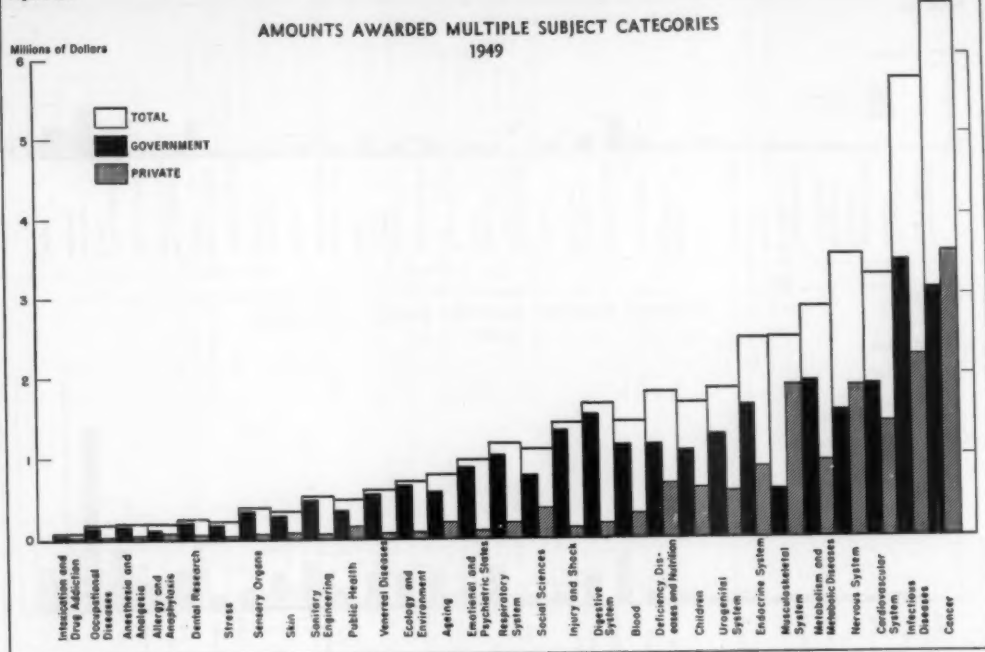


Figure 12e

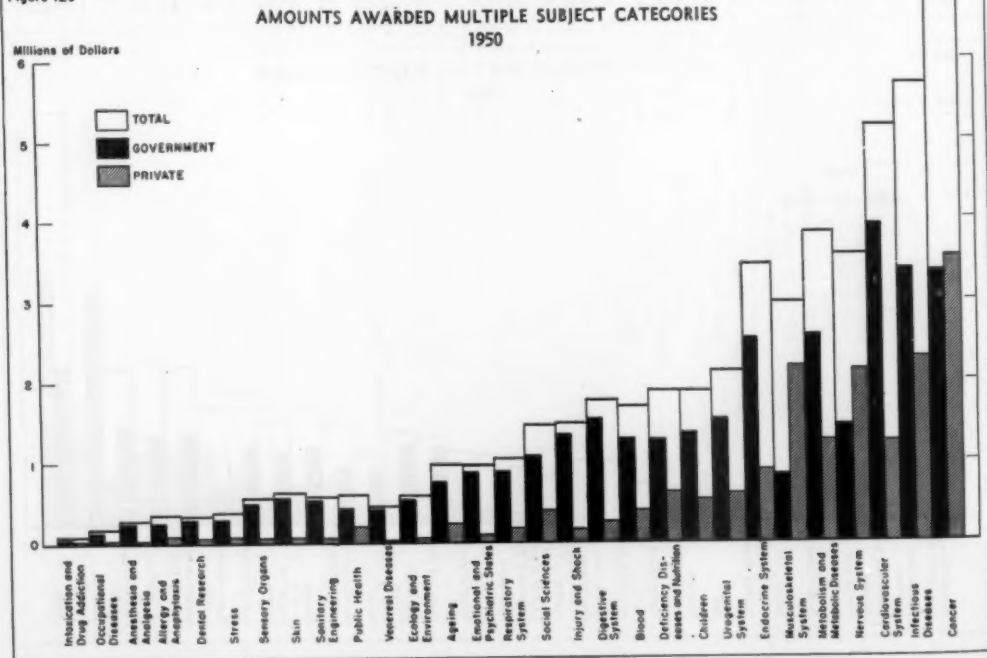
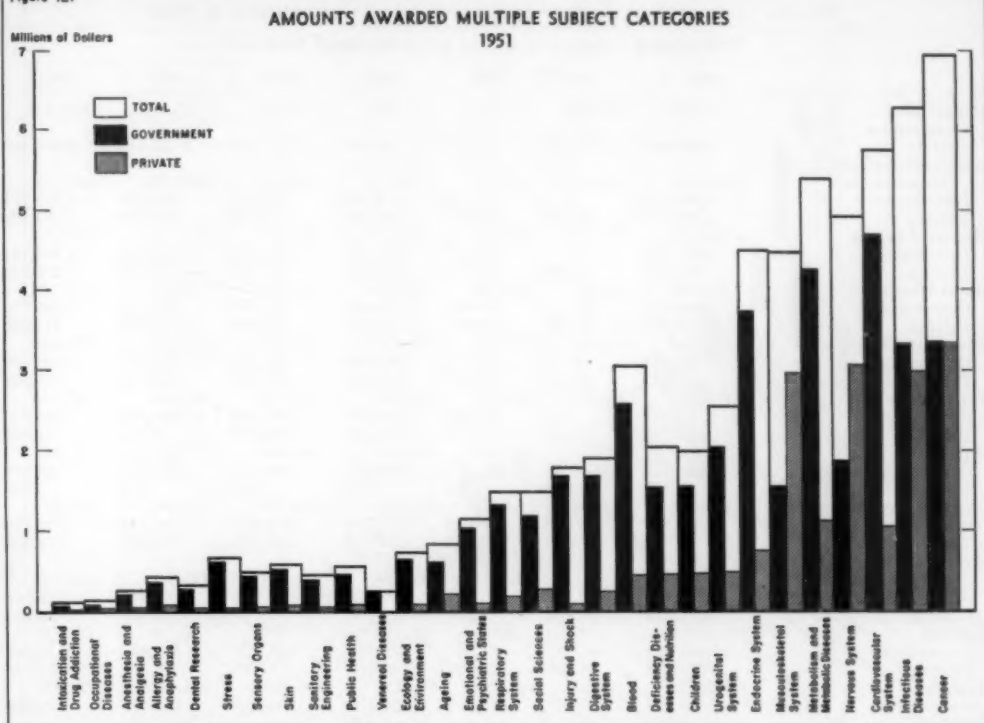


Figure 12f



the most heavily supported fields also contribute substantially to knowledge in other fields.

The amounts awarded the multiple subject categories during the total period and for each year concerned are presented in Figs. 12-12f. Particular diseases and conditions which received amounts of 1 million dollars or more throughout the period are shown in Table 10. Although cancer, as a disease, might logically belong to this group, it does not appear in the table. As a major category it comprises basic studies of such variety that direct comparison with subtopics of other categories is not possible.

The exchange maintains detailed information on the distribution of funds within the major multiple categories, but this detail is of such volume that it does not lend itself to reproduction in a paper of this nature. The emphasis within some of the major categories with which we have been dealing is briefly outlined as follows. Within the Blood System, cancer, chiefly leukemia, and the anemias have each received more than 1 million dollars of the 7 million total. In Cancer, approximately half the 27 million dollars has been granted to studies concerned with carcinogenesis and therapy. In the Cardiovascular System, emphasis has been placed in the following order: arteriosclerosis and hypertension, heart disease, and rheumatic conditions (which have merited a special topic).

The Problems of Children embrace many studies of diseases which in the aggregate represent a fair percentage of the funds, but which individually are relatively meagerly supported as compared to the support of studies dealing with Mental Health of the Child or Pregnancy and the Newborn. Under the Digestive System, liver diseases, cancer, and enteric infections have received major support. Research on the Endocrine System falls into three groups: diseases of the endocrine system proper, which are not heavily supported, the role of the endocrines in cancer on which nearly 3 millions have been spent, and the role of the endocrines in other diseases to which 9 millions have been awarded.

Among the Infectious Diseases, poliomyelitis outranks all others, with tuberculosis second, syphilis third, and malaria fourth. The single source of funds for research in poliomyelitis represents an outstanding example of the role of a nongovernment agency in accepting the whole support of a particular disease. In the field of Metabolic Studies, metabolic diseases receive less emphasis than basic studies or the role of metabolism in other diseases. Diabetes, however, has received such substantial support during the past several years that it is among those diseases supported in amounts greater than 1 million dollars.

Within the Musculoskeletal System, basic research

TABLE 10
SPECIFIC AREAS OF RESEARCH SUPPORTED IN THE AMOUNT OF 1 MILLION OR MORE

	Total amount		Amounts by fiscal year				
	1946-51	1946	1947	1948	1949	1950	1951
Poliomyelitis	7,331,825	242,186	491,918	746,267	1,513,123	1,729,027	2,609,304
Government	—	—	—	—	—	—	—
Private	7,331,825	242,186	491,918	746,267	1,513,123	1,729,027	2,609,304
Arteriosclerosis and Hypertension	4,859,905	83,118	445,180	604,773	900,438	1,229,359	1,597,037
Government	3,509,381	—	258,326	408,726	546,810	980,221	1,315,298
Private	1,350,524	83,118	186,854	196,047	353,628	249,138	281,739
Kidney Diseases	4,321,241	53,090	338,850	524,427	825,870	1,059,929	1,519,075
Government	3,476,324	—	227,150	418,745	648,052	873,226	1,309,151
Private	844,917	53,090	111,700	105,682	177,818	186,703	209,924
Heart Disease	3,282,030	58,026	218,029	315,923	494,998	1,018,278	1,176,776
Government	2,618,391	21,231	130,915	235,624	272,016	893,335	1,065,270
Private	663,639	36,795	87,114	80,299	222,982	124,943	111,506
Rheumatic Conditions	2,787,115	45,165	199,653	310,137	612,695	804,006	815,409
Government	1,357,642	—	84,126	165,389	156,530	359,517	592,080
Private	1,429,473	45,165	115,527	144,798	456,165	444,489	223,329
Tuberculosis	2,666,595	30,331	229,228	656,749	817,049	545,539	387,699
Government	2,229,956	—	204,647	528,384	647,384	493,704	355,837
Private	436,639	30,331	24,581	128,365	169,665	51,835	31,862
Syphilis	2,373,412	276,657	621,405	536,841	441,045	345,820	151,644
Government	2,366,912	276,057	620,805	536,241	440,445	345,220	148,144
Private	6,500	600	600	600	600	600	5,500
Pregnancy and Newborn	1,795,655	61,765	205,468	309,816	430,135	391,943	396,528
Government	1,223,857	34,565	139,634	181,740	262,259	283,134	322,525
Private	571,798	27,200	65,834	128,076	167,876	108,809	74,003
Liver Disease (Excluding cancer)	1,784,745	31,467	65,337	326,368	422,520	423,246	515,807
Government	1,714,459	25,267	61,337	315,818	400,784	408,646	502,607
Private	70,286	6,200	4,000	10,550	21,736	14,600	13,200
Diabetes	1,350,067	6,700	50,380	187,319	297,463	380,766	428,049
Government	1,073,639	—	25,580	141,908	242,622	309,985	353,544
Private	277,028	6,700	24,800	45,411	54,841	70,771	74,505
Malaria	1,320,990	50,800	269,416	325,422	298,366	245,097	131,889
Government	1,315,490	50,800	269,416	322,422	298,366	242,597	131,889
Private	5,500	—	—	3,000	—	2,500	—
Enteric Infections	1,260,897	48,471	196,943	208,727	284,366	290,072	232,318
Government	1,223,117	48,471	196,943	203,047	273,466	271,372	229,818
Private	37,780	—	—	5,680	10,900	18,700	2,500
Studies on the Eye	1,179,035	19,150	69,059	122,048	193,742	380,737	394,299
Government	980,301	4,150	39,059	80,648	156,462	350,093	349,889
Private	198,734	15,000	30,000	41,400	37,280	30,644	44,410
Upper Respiratory Infections	1,151,526	29,075	197,796	206,092	278,678	176,100	263,785
Government	1,063,126	15,800	181,786	187,527	251,608	171,850	254,555
Private	88,400	13,275	16,010	18,565	27,070	4,250	9,230
Arthritis and Degenerative Joint Diseases	1,146,113	78,000	49,320	69,075	226,561	248,343	474,814
Government	614,153	—	10,320	14,500	82,362	105,589	401,382
Private	531,960	78,000	39,000	54,575	144,199	142,754	73,432
Mental Health of Children	1,099,744	5,000	900	260,817	229,482	268,669	334,876
Government	954,348	—	—	156,317	214,806	266,169	317,056
Private	145,396	5,000	900	104,500	14,676	2,500	17,820
Anemias	1,082,686	68,570	110,320	192,302	187,530	213,985	309,979
Government	818,663	56,070	54,860	148,552	133,755	169,227	256,199
Private	264,023	12,500	55,460	43,750	53,775	44,758	53,780

on bone and joint and studies on arthritis and degenerative joint diseases received the major support; muscular atrophy and dystrophy were in second place, with fractures and bone surgery third. Paralytic conditions are far in the lead among studies of the Nervous System, with basic studies and convulsive disorders following in that order.

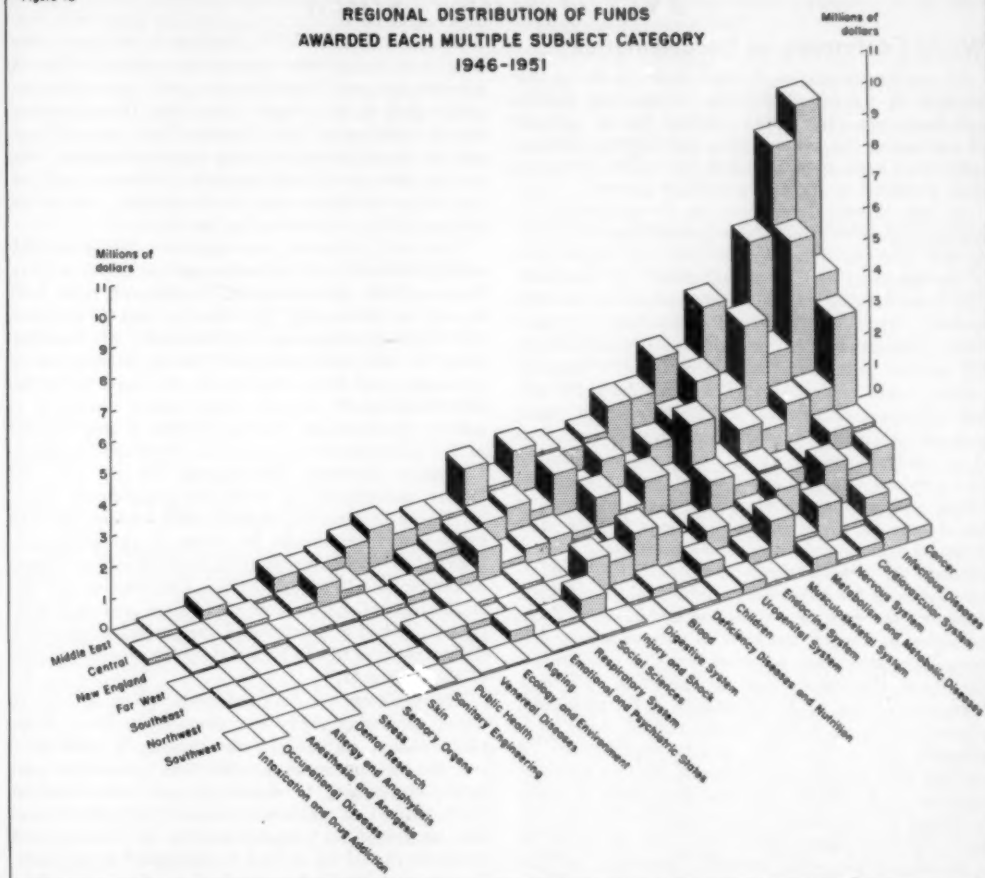
Within the Respiratory System, great emphasis has been placed upon upper respiratory infections, which have received approximately 1 million dollars,

whereas all other respiratory diseases, including pulmonary tuberculosis, have been supported in the amount of 2.7 million.

With the exception of the eye, the Sensory Organs are poorly supported. Studies on the eye have had nearly 66% of the total available for all sensory organs. Within the Urogenital System, kidney disease is of the first order of magnitude, with cancer in second place. Venereal disease has not been included within this system.

Figure 13

REGIONAL DISTRIBUTION OF FUNDS AWARDED EACH MULTIPLE SUBJECT CATEGORY 1946-1951



The final approach to the multiple category material was the determination of the direction of research interest in the various regions. Fig. 13 illustrates this apportionment of funds. Only those research areas receiving the lowest support are not represented in all regions. It would appear that interest in every research field is nation-wide and that regional dispersion within categories follows closely that of total funds.

The review of this body of data, probably the largest accumulation of its kind maintained on a current basis, represents the first major report of the Medical Sciences Information Exchange. The data are, we believe, sufficient to permit the following conclusions:

1. Increasing governmental support of medical research has not diminished funds from private sources.
2. Geographically, the support of medical research by government and private sources is widely distributed and is in conformance with research potential.

3. There is no evidence of unreasonable duplication of research support by government and private agencies. Each source contributes to a substantial number of institutions not supported by the other, although there is mutual support of established institutions.

4. Most grants are small; 68% are in amounts below \$10,000.

5. Support is widely distributed among investigators; 75% of them have received, over the six-year period, amounts which fall below the \$37,000 mean or, in other words, an average of less than \$6,000 in any one year.

6. The evidence shows that the annual grant system has provided continuity of support. At least 50% of all projects are receiving a minimum of three years of support.

7. The support of medical research is distributed among a wide variety of subject fields.

8. Our experience indicates that the extensive interrelationships among the fields of research spread the influence of the support of generously supplied areas well beyond the major fields of interest.

News and Notes

World Conference on Documentation

IN documentation, as in other fields of study, subdivision of subject matter has become unavoidable, and documentalists, getting together for the purpose of organizing the accumulation and dissemination of specialized knowledge, now find themselves discussing their problems in strictly specialized groups.

At the World Conference on Documentation in Rome, September 15-21, the proceedings were subdivided into the following sections: (1) application of the universal decimal classification; (2) documentary reproduction methods and mechanical selection devices; (3) bibliography and abstracting; (4) auxiliary publications; (5) training of documentalists; (6) general problems of classification; (7) linguistic problems and terminology. None will deny the wisdom of this arrangement, which allows each group to dispense with preliminaries and start deliberations at precisely the point where they were discontinued on a previous occasion. If, however, there was a slight feeling of disappointment among some delegates, it was due to the timetable, which made it impossible to attend as many meetings as one might have wished, although the plenary session at the end of the conference made up for any gaps in individual attendances.

During the past few years the emphasis of documentation as a whole has been on natural science and technology rather than on other branches of learning. The Rome Conference was no exception; although there were papers on documentation in the social and economic sciences, public administration, local government, and so on. The specific requirements of archives were more strongly stressed than on previous occasions, and definite proposals were made in favor of setting up documentation centers for the humanities along lines comparable to those now operating in, or in conjunction with, scientific, technical, and industrial libraries.

The conference was jointly arranged by the Fédération Internationale de Documentation (FID) and the Consiglio Nazionale delle Ricerche (CNR), which also shared the burden of technical preparations, printing of papers, interpreting, and secretarial services. Offprints were contributed by some French, Swedish, German, and Austrian periodicals; and a special number of *American Documentation*, with papers by Vernon Tate (editor), Keyes D. Metcalf, Lester K. Born, Watson Davis, Fremont Rider, and others, was also distributed to the delegates.

In view of the total of a hundred or more formal papers, it was impracticable to discuss each of them separately, and the time available for discussion was devoted to a limited number of selected problems. In Section 1 these included the question of authorities responsible for publicizing and explaining the principles and applications of the Universal Decimal Classification, the compilation of a list of UDC users, and the distribution of the new cumulative extensions

and corrections of UDC. Section 2 set up a symposium to discuss the comparative merits of different microtechniques. Those taking part were Fremont Rider and E. B. Power, from the United States; M. G. Cordonnier, from France; and Lucia Moholy and R. S. Schultze, from the United Kingdom. The section also considered questions of format and terminology, but there was no opportunity for an exchange of views on selection devices.

Section 3, following a recommendation of the Scientific Information Conference at the Royal Society, London, 1948, considered the drafting of rules, with a view to uniformity, for citations and descriptions of references; discussed the possibility of standardizing the bibliographical and formal presentation of abstracts; and drew attention to the need for better dissemination of technical information contained in patent specifications. Section 4 took a step further in the direction of work done at the American Documentation Institute, Washington, D. C., and the Centre national de la recherche scientifique, Paris, by urging that scholarly production existing only in typescript form should be listed in analytical bibliographies with indication of the depository library or center able to supply copies. Universities and scientific institutions were urged to have academic writings published or reproduced for exchange purposes, such exchanges not to be based on the monetary value of the document.

The training of documentalists (Section 5), to which particular study was devoted by Mme. Briet (Bibliothèque nationale), was thoroughly gone into, and the section recommended that prototype programs of training be drawn up and documentation be recognized as a profession in its own right. It was also suggested that representatives of archives and museums should be invited to take part in any conference that might be convened in this connection. Section 6 considered the different systems of classification now used in libraries, archives, documentation centers, and government offices, and expressed the hope that possibilities of coordinating the different systems might be explored. Section 7 recommended the standardization of lexicographical principles, the compilation of terminological bibliographies and directories of organizations dealing with terminological matters, and various other steps leading to the production of specialized vocabularies, to be organized by national and international agreement under the auspices of Unesco.

As an adjunct to the conference, the organizers provided for an exhibition of bibliographical and technical tools at the Istituto di Matematica at the Città Universitaria. The general scope of the exhibition did not differ appreciably from earlier displays in Great Britain and other European countries, but it brought home to us, if we did not know it already, that technical means of documentation are now a

sine qua non. There is, moreover, need for the use of many different methods, and the questions today are not silver salts or dyeline, notches or punches, films or microcards, mechanical or electronic selection. What matters is acquaintance with the various methods, appraisal of their specific usefulness for different purposes, and guidance in how to apply them to the best advantage. Technical aids, if carefully selected and coordinated, can assist research programs and be of great value to the ultimate aim of modern documentation: to keep men of science and scholars currently informed of all the literature pertaining to their respective subjects.

The conference was attended by some 350 delegates and observers from 31 countries and several supranational agencies, including Unesco, the Food and Agricultural Organization, the International Labour Office, and the Organization for European Economic Cooperation.

LUCIA MOHOLY

Documentation Service
London, England

Scientists in the News

Mary L. Alexander, assistant to the director of research, Universal Oil Products Co., has been appointed chairman of the Committee on Nomenclature, in the American Chemical Society's Division of Organic Chemistry. The first woman to occupy the post, Miss Alexander was chosen because of her expert knowledge of chemical literature in organic and petroleum chemistry.

Clifford E. Berry, authority in the field of mass spectrometry, has been promoted to the office of assistant director of research at Consolidated Engineering Corporation, of Pasadena. Dr. Berry joined Consolidated in 1942 as research physicist, later becoming chief physicist.

Nathan Birnbaum, on leave of absence as associate professor of chemistry at the City College of New York, is deputy chief of the Research and Development Division in the Office of the Chief Chemical Officer, Washington, D. C. Lt. Colonel Birnbaum was formerly stationed at Army Chemical Center, Md., and was in charge of Chemical Corps participation during the Operation Greenhouse atomic weapons test at Eniwetok.

Lindsay M. Black, curator of plant pathology at the Brooklyn Botanic Garden, has been appointed professor of botany at the University of Illinois, effective Sept. 1. Dr. Black will take charge of a new program of teaching and research in plant pathology.

N. W. Conner has been appointed director of the Department of Engineering Research in the School of Engineering at State College, North Carolina. Professor Conner has been acting head of the department since last fall, when W. G. Van Note resigned to be-

come president of Clarkson College of Technology in Potsdam, N. Y. He has been a member of the State College faculty since 1937.

William E. Doering, member of the Columbia University faculty since 1943, has been named professor of organic chemistry at Yale University. He will join the Yale faculty on July 1. Professor Doering accomplished the synthesis of quinine during World War II while working with Robert B. Woodward, of Harvard.

Lloyd H. Donnell has been appointed acting chairman of the Department of Mechanics at Illinois Institute of Technology. He will head the department for one year in the absence of William R. Osgood, who is on a year's leave of absence to edit a monograph on residual stresses in metals and metal structures for the National Research Council. Mr. Donnell has been at Illinois Tech since 1939.

Thomas J. Fricke and Raphael G. Kazmann have joined their offices and are now undertaking work as a partnership under the name Fricke and Kazmann, Consulting Engineers, at Stuttgart, Ark. They will specialize in the integrated development of surface and ground-water supplies.

Newell S. Gingrich, professor of physics, has taken sabbatical leave from the University of Missouri to work with the Oak Ridge National Laboratory Physics Division.

Milton C. James has retired as assistant director of the Fish and Wildlife Service. He will be succeeded by John L. Kask, who, since 1948, has been chief biologist of the Fisheries Division of FAO. Mr. James has been a member of several international fisheries commissions and has acted as deputy administrator of the Defense Fisheries Administration since its establishment in December 1950. He became a permanent employee of the former Bureau of Fisheries in 1923, when he was appointed as scientific assistant to work on fish hatchery problems. In June 1942 he was made chief of the Division of Fish Culture, and in September 1945 he became assistant director.

Uerner Liddel, director of the Division of Physical Sciences, ONR, has been appointed chief of the AEC Physics and Mathematics Branch, Division of Research. Dr. Liddel entered the Navy in 1942 and was assigned to ONR as head of its Physics Branch in 1946. He holds the rank of Commander. In his new post, he will be responsible for the development and supervision of programs of fundamental and applied physics and mathematics research in AEC laboratories and in universities and other institutions outside the AEC.

G. C. McVittie, professor of astronomy at Queen Mary College, University of London, has been appointed professor of astronomy at the University of Illinois. He will probably come to the U. S. this summer.

The Western Union Telegraph Company has announced the appointment of **Leon G. Pollard** as electronics research engineer in charge of its laboratories at Water Mill, L. I. **William D. Buckingham** was appointed assistant electronics research engineer to succeed him. Mr. Pollard succeeds the late **Edward C. Homer**.

Henry G. Poncher, professor of pediatrics and head of the department at the University of Illinois College of Medicine, has resigned to enter private practice in Valparaiso, Ind. He has also accepted a part-time position as medical director and as visiting professor in human biology at Valparaiso University. Dr. Poncher has been associated with the University of Illinois since 1928.

Russell S. Poor, chairman of the University Relations Division of the Oak Ridge Institute of Nuclear Studies, has taken a year's leave of absence to join the National Science Foundation. Dr. Poor will head the NSF Research Education Section of the Division of Scientific Personnel and Education.

M. N. S. Rao and **S. N. Sengupta**, assistant geophysicists in the Geological Survey of India, are in this country to acquire practical experience in field geology and geophysics. They plan to be here for one year.

Hans H. Reese, president-elect of the American Neurological Association, has been appointed chairman of the Medical Advisory Board of the National Multiple Sclerosis Society for a two-year term. Dr. Reese is professor of neurology and psychiatry of the University of Wisconsin Medical School and chief of its Department of Neuropsychiatry. Newly appointed vice-chairman of the society's Medical Advisory Board is **Richard M. Brickner**, assistant clinical professor of neurology, College of Physicians and Surgeons, Columbia University. Dr. Brickner is also associated with Mt. Sinai Hospital of New York City. **Tracy J. Putnam**, formerly chairman of the Medical Advisory Board, has been appointed honorary chairman. Dr. Putnam is chief of the Department of Neurosurgery, Cedars of Lebanon Hospital, Los Angeles.

Randal McGavock Robertson has been appointed science director of the Office of Naval Research, succeeding **Thomas J. Killian**, who recently was named chief scientist of the Office of Ordnance Research at Duke University. Dr. Robertson will be responsible for the scientific contract research program sponsored by ONR. Before joining the ONR staff in 1946, he was associated with the Radiation Laboratory at MIT.

S. Wyman Rolph, president of the Electric Storage Battery Company, was elected president of the Franklin Institute at the annual meeting of the institute's Board of Managers. The retiring president, **Richard T. Nalle**, president of the Midvale Company, was appointed to the Board of Managers to fill Mr. Rolph's unexpired term. Mr. Nalle had been president of the institute since 1946. **Morton Gibbons-Neff**, Philadel-

phia insurance broker, was elected a vice president of the institute, and **E. G. Budd, Jr.**, of the Budd Company, and a retiring vice president, was named to the board. **C. M. Waterbury** was elected assistant treasurer.

Charles S. Simons, associate professor of physics at Louisiana State University, has joined the Oak Ridge Institute of Nuclear Studies as a senior scientist in the Special Training Division. Dr. Simons, who directed the LSU Radiochemical Laboratory in addition to his work in the Physics Department, will be associated with the conduct of the radioisotope techniques courses and other offerings.

C. Richard Soderberg, of Massachusetts Institute of Technology, has been awarded the John Ericsson Gold Medal for 1952 by the American Society of Swedish Engineers in New York. The medal is awarded every other year to a Swede or an American citizen of Swedish descent, in recognition of extraordinary merit in technological or scientific fields. Dr. Soderberg was born at Ulvöhamn in northern Sweden and graduated from Chalmers Institute of Technology in Gothenburg. In 1938 he accepted a professorship in applied mechanics at MIT, and since 1947 he has been head of the department.

Calvin B. Spencer has been appointed chief of the Division of Foreign Quarantine, USPHS, and **Gilbert L. Dunnahoo** has been made chief of Medical Programs, FSA Region X, San Francisco. Dr. Spencer, who succeeds Dr. Dunnahoo as chief of Foreign Quarantine, has been with PHS for 23 years. In 1948, he was appointed chief quarantine officer for the Port of New York, where he served until his present assignment. As chief of Medical Programs for FSA's Region X, he will be responsible for programs on tuberculosis control, venereal disease, heart disease, cancer, environmental health, and public health nursing which are now being operated in cooperation with the states and territories. Region X includes California, Arizona, Nevada, Oregon, Washington, Hawaii, and Alaska.

Robert Stokstad, of the nutrition and physiology section of Lederle Laboratories, has received England's Tom Newman Memorial Award for 1951. The award is given by the Poultry Association of Great Britain for the most important contribution in poultry husbandry research. Dr. Stokstad made important advances in studying the role of aureomycin, vitamin B₁₂, and folic acid in nutrition.

Itiro Tani, professor of fluid mechanics at the University of Tokyo, has joined the Cornell University staff as visiting professor in the Graduate School of Aeronautical Engineering. Dr. Tani, who is supported by a traveling fellowship from the Japanese government, will be at the university for at least six months. Dr. Tani has worked more than 20 years in aerodynamic research. The main purpose of his visit to the U. S. is to obtain a closer acquaintance with current research and development in aeronautical engineering.

Gordon S. Taylor has joined the plant pathology

staff of the Connecticut Agricultural Experiment Station. He has spent the past four years at Iowa State College, where he served as a graduate assistant in plant pathology. Mr. Taylor was employed by the station's Plant Pathology Department during the summer of 1947, after his graduation from the University of Connecticut.

C. F. Tipper, senior lecturer in mechanical engineering at Cambridge University, will work for several months in the Mechanics Division of the Naval Research Laboratory. Dr. Tipper has been active in the field of brittle fracture of steel.

William W. Trench, secretary of the General Electric Company for nearly 24 years, has retired. He has been secretary of the company's board of directors and its advisory committee and has been a trustee or member of the board of all financial subsidiaries and trusts.

Esther P. Walcott, of Washington, D. C., until recently a case worker for the Connecticut Commission on Alcoholism, has been appointed assistant professor of social work at West Virginia University. She is a former case consultant for the Family Society of Syracuse, N. Y., and instructor at Syracuse University.

Bernard B. Watson has been appointed professional and scientific personnel specialist of the Labor Department's Defense Manpower Administration. He has served as specialist for physics in the Division of Higher Education of the U. S. Office of Education since 1949 and has been active on the AAAS Cooperative Committee on the Teaching of Science and Mathematics. Dr. Watson will be responsible for programs involving scientific, engineering, and other specialized personnel.

F. H. Wells, of the Atomic Research Establishment, Harwell, Eng., spent February 13-15 consulting with the personnel of Radiation Counter Laboratories, Inc., at their new laboratory in Skokie, Ill.

Education

Boston College will hold a special intensive course in Modern Industrial Spectrography July 21-Aug. 1, designed primarily for industrial chemists and physicists. Further information may be obtained from James J. Devlin, of the Physics Department.

The **Committee for Economic Development** has received a grant of \$123,750 from the Fund for Adult Education, which it will use to help support the activities of the Joint Council on Economic Education, a nonprofit organization. The council's principal activity, since its founding in 1949, has been assistance in the organization of workshops under institutional sponsorship at which high school teachers and administrators, leaders in education, business, labor, and government try to develop methods of improving classroom instruction in economics. More than 2400 teachers have attended the workshops.

In a **Farm Youth Exchange** program, eight young men and women from as many states flew to San Juan in February for a six weeks' study of social and economic conditions in Puerto Rico. After spending several days at the University of Puerto Rico, the group traveled with agricultural extension leaders, and then spent four weeks living and working on some of the larger sugar, coffee, and coconut farms. In a return program, 12 young Puerto Rican farmers will come to this country early this summer to live and work on U. S. farms.

A course in "The Methods of Science" will be offered July 1-Aug. 15 in the **Harvard Summer School** by James B. Conant, assisted by Fletcher Watson, of Harvard, and Paul F. Brandwein, head of the Science Department, Forest Hills (N. Y.) High School. The course will follow President Conant's "case history" method of teaching how scientists work. A number of scholarships are being offered.

The **University of Illinois**, under the direction of John C. McGregor, will send student expeditions to archaeological sites in Illinois in a search for new facts about the Hopewell culture. Last year and in 1949 the expeditions worked in Arizona, in cooperation with the Museum of Northern Arizona.

Lehigh University is planning to install, in cooperation with Bethlehem Steel Company, the world's largest vertical universal testing machine in a new building to adjoin Fritz Engineering Laboratory. The building, which will be completed in 1954, will house a 5,000,000-lb. hydraulic tension compression machine, a 20-ton overhead crane, a 30' x 100' testing platform, other accessory equipment, and laboratories. William J. Eney is head of the laboratory and of the Department of Civil Engineering and Mechanics. Lehigh will offer a new curriculum in September in the College of Engineering, for the preparation of high school teachers, which will place increased emphasis on science and mathematics.

Massachusetts Institute of Technology has appointed Max F. Millikan, professor of economics, director of the newly established Center for International Studies, which was created to meet the need for the intensive study of world affairs in the fields of social, political, and natural science, as well as in economics. The Advisory Board of the center is composed of Julius A. Stratton and John E. Burchard, of MIT; Paul H. Buck and Edward S. Mason, of Harvard; and Henry M. Wriston, president of Brown University.

Additions to the faculty of the **University of Michigan Biological Station** at Cheboygan include Lloyd H. Shinnars, of Southern Methodist University (taxonomy of flowering plants); Frederick K. Sparrow (lower fungi and the aquatic flowering plants); and Warren H. Wagner, Jr. (fresh-water algae), who will introduce a new course in pteridophytes and gymnosperms. Margaret H. Fulford, of the University of Cincinnati, will conduct a new course in lichens, as well as a course in bryophytes and research in both

fields. Frank C. Gates, of Kansas State, will be in charge of the work in plant ecology. Also new on the faculty is John T. Emlen, of the University of Wisconsin, who will work with Olin S. Pettingill, Jr., in ornithology. Clarence H. Kennedy, professor emeritus, Ohio State, will continue his investigations on Northern ants, and other study and research will also be continued.

The University of North Carolina has named Clifford P. Lyons dean of the College of Arts and Sciences to succeed William Wells, who resigned last fall. Arthur Roe, chairman of the Division of Natural Sciences, was appointed head of the Chemistry Department to succeed Ralph W. Bost, who died in September. Roger W. Howell, of the University of Minnesota Medical School, has been appointed head of a new department, Mental Health, in the School of Public Health.

A new pharmacology laboratory has been completed at North Dakota Agricultural College. It will enable advanced pharmacy students to do actual experimental work where previously only demonstration was possible.

The fourth annual Oak Ridge Summer Symposium, Aug. 25-29, will consider "The Role of Atomic Energy in Agricultural Research." Sessions will be devoted to plant and animal studies with atomic energy research tools, in addition to sessions on carbon 14. For additional information, write to University Relations Division, P. O. Box 117, Oak Ridge, Tenn.

The University of Tennessee College of Medicine will award a prize to the member of each graduating class "who has overcome the most difficulties in obtaining a degree," regardless of his scholarship record. A committee of his classmates, with the aid of F. J. Montgomery, director of student welfare, will select the prize winner. The prize has been underwritten by Charles C. Verstandig, of New Haven, Conn., a 1939 alumnus.

Honduras and Nicaragua will be the locale of the third University of Texas Geography Field School in Latin America, June 15-Aug. 23. The course is restricted to male students of junior or, preferably, senior or graduate, status with appropriate scientific training. For application forms and further information, write to Dan Stanislawski, Department of Geography, Austin 12, Texas. Enrollment is limited, and applications will not be considered after May 1.

At the University of Wisconsin the Department of Social Work has become the School of Social Work. Arthur P. Miles, chairman of the department, has been made its first director.

The Yale University Silliman Lectures will be given this year by Hans Pettersson, director of the Oceanografiska Institutet, Göteborg, Sweden, on Apr. 16, 17, 18, 21, 22, 24, and 25, on the general topic "The Ocean Floor and its Problems." The lectures will be illustrated and open to the public.

Grants and Fellowships

The Ernst Bischoff Award of the American Association of Clinical Chemists, Inc., will be presented annually to a chemist on the staff of a hospital or clinical chemistry laboratory "who has distinguished himself by achievement . . . and has helped to solve those chemical problems which arise daily in the practice of the medical arts." A cash prize, a scroll, and a bronze medal will go to each recipient. Harry Sobotka, of Mount Sinai Hospital, New York, is chairman of the first Award Committee, which will announce its decision at the annual meeting of the association, Apr. 2, in Milwaukee.

Grants from the Gans Fund, of Bethany College, have been made for scientific research to Esther L. McCandless, of the Women's Medical College of Pennsylvania, and Irving A. Tittler, of Brooklyn College.

Applications for General Electric Science Fellowships at Case Institute of Technology, Cleveland 6, must be submitted to Elmer Hutchisson of the institute, by Apr. 11. The summer session will be held June 23-Aug. 1 and is open to 50 physics teachers from Ohio, West Virginia, Kentucky, Indiana, Illinois, Wisconsin, Michigan, Mississippi, Tennessee, Iowa, Minnesota, and western Pennsylvania. General Electric fellowships at Union College and Rensselaer Polytechnic Institute are not available after Apr. 1.

The Great Northern Paper Company has subscribed \$5,000 toward the scholarship fund of the University of Maine Pulp and Paper Foundation, which, established two years ago, provides loans and scholarships, interests students and men from industry in advanced study, screens outstanding students for the five-year operational management program, and works to advance fundamental and applied research.

The Eli Lilly Company has awarded a grant to the University of Georgia School of Pharmacy to permit Joseph P. La Rocca and Woodrow R. Byrum to continue their studies of sedative hypnotic drugs. They expect to synthesize a new series of pharmaceutical compounds and explore their pharmacological action.

One fellowship, for \$1500, and several research assistant- and associateships for graduate study in the Department of Metallurgy are offered by MIT. Half-time research assistants may receive \$90-\$100 per month, plus all or part tuition; full-time research assistants, \$180-200 per month, plus all or part tuition; and research associates, \$250-\$400 per month. The program is sponsored by Armour and Company, the Atomic Energy Commission, and the Engineering Foundation. For full information, write to A. M. Gaudin, Room 8-209, Cambridge 39, Mass.

National Science Foundation travel grants, the first to be made, went to John R. Kline, Saunders MacLane, Einer Hille, and Gordon P. Whyburn to permit their attendance as members of the U. S. delegation at the

first General Assembly of the International Mathematical Union in Rome, March 6-8.

The **National Science Teachers Association** will administer a Program for Future Scientists, Engineers and Technicians for the American Society for Metals. Awards will include funds for scholarships, libraries, and laboratory equipment, certificates of achievement, and plaques for schools and science teacher associations. The program is open to students in the seventh to twelfth grades, inclusive, science teachers, schools, science departments, and science teacher associations. For full information write to NSTA Committee on Awards, 1201 16th St., N.W., Washington 6, D. C.

The **National Society for Crippled Children and Adults** and **Alpha Gamma Delta**, international women's fraternity, will sponsor a training course in work with the severely crippled, in New York July 9-Aug. 8. Grants will total approximately \$300 each, including tuition and room and board. Applications, returnable by Apr. 1, may be obtained from the society's National Personnel Registry and Employment Service, 11 S. La Salle St., Chicago 3.

In the Laboratories

Corning Glass Works will construct a new plant in Harrodsburg, Ky., to meet the increasing demands of the armed forces for optical glass for military purposes. Harry S. Sterling, production superintendent at the main plant, has been appointed manager of the new plant, which is expected to be completed this year.

Du Pont plans to build a \$2,000,000 Haskell Laboratory of Industrial Toxicology near Newark, Del. In addition to expanded research on potential industrial hazards associated with Du Pont products and processes, the company will engage in basic research on the causes of industrial fatigue and the factors that make clothing comfortable, in a special all-weather room. In the Falling Waters-Beddington section along the Potomac River near Martinsburg, W. Va., a 50-building commercial explosives plant is being constructed. Operations will probably begin early in 1953.

Koppers Company, Inc., has added four chemists to the staff of the Research Department of its experiment station in Verona, Pa.: Arnold E. Jeltsch, of Procter & Gamble; William E. St. Clair, of the Naval Stores Research Division, Olustee, Fla.; Michael E. Dufala, of the Erie Resistor Corporation; and Norman S. Boodman, of the Vitro Manufacturing Co.

Organizational changes in the **Lilly Research Laboratories** include the appointment of A. H. Fiske as vice president in charge of the new Development and Control Function. E. C. Kleiderer was appointed executive director of Development, and W. J. Rice was named to the same position for Control. H. C. Miller has become director of the Development Divi-

sion, and M. D. Bray succeeds him as head of the Pharmaceutical Research Department. The Research Function is now under the supervision of two associate directors, J. A. Leighty and R. M. Rice. Other appointments include directors of the following divisions: Organic Chemical Research, T. P. Carney; Biochemical Research, O. K. Behrens; and Physicochemical Research, W. W. Davis.

Arthur D. Little, Inc., has added the following staff members to various divisions: Wilbur Cox, Robert Harrison, Marian Hawes, Charles Jenest, Claire Richards, and Janice Rossbach. Howard O. McMahon has been appointed to the new post of science director. In this position he will serve as adviser to Little officers, but will not be responsible for assignment or execution of research projects, nor for administration of personnel.

A section of the inorganic research activities to the **Monsanto Chemical Company** Phosphate Division will be transferred from Anniston, Ala., to Dayton, Ohio. New laboratories and other facilities were completed late in February. John Van Wazer, assistant research director, will be in charge of the section, and T. W. Schilh, J. S. Metcalf, and P. G. Arvan, research group leaders, will move to the new location.

Parke, Davis & Company's extension of its facilities during the next five years will include the new plant being completed at Holland, Mich.; new laboratories in Buenos Aires, Australia, Havana, Canada, and at several other domestic and foreign locations; enlargement of the Mexican and the Detroit plants; new research facilities; and a new medical center. The company also expects to manufacture some of its products in India, Germany, Japan, and Italy.

Meetings and Elections

A **Conference on College-Community Relations for Functional Education**, sponsored by Columbia University, the College of the City of New York, and Barnard College, will be held Apr. 24-25. The conference is open to all Eastern colleges interested in problems of functional education and to representatives of agencies concerned with undergraduate education or its meaning to local communities. Address all inquiries to the chairman of the conference, 209 Millbank Hall, Barnard College.

The **Conservation Council for Hawaii**, composed of representatives of 25 federal, territorial, and private agencies interested in various phases of conservation, has elected the following officers: president, H. A. Wadsworth; vice president, Alice S. Brown; secretary, E. C. Zimmerman. Chairmen of standing conservation committees are: Max Carson, Water; Walter Sykes, Land; Colin Lennox, Flora; Vernon Brock, Fauna; and Mrs. Brown, Sites (archaeological, historical, and scenic). Council accomplishments during the past year through its standing committees include: work on preservation of the Ulupo heiau on Oahu; stimulation of interest that led to clearing away and rededica-

tion of Keaiwa, the unique medical *heiau* at Aiea, Oahu; arrangements to prevent the destruction of a *Antidesma kapuae* stand and other valuable native flora in South Kona, Hawaii; recommendation for the creation of a sanctuary of three or four acres at Kapulehu in North Kona, Hawaii, to protect native trees typical of this dry area. An open list of diminishing species of native plants has been compiled and distributed. Action was taken to prevent denudation of beaches in the islands caused by removal of sand for commercial purposes. During the Science Symposium held by the Hawaiian Academy of Science, a resolution, sponsored by the council, was adopted by the academy. It requested the study of the project to import axis deer (*Cervus axis*) to the island of Hawaii and that legislation be enacted to make it illegal to transport deer from one island to another until a suitable survey had been made. Since this action the project for placing axis deer on Hawaii has been in abeyance.

The fourth **Institute of Northwest Resources** will be held on the Oregon State College campus June 23-July 5. Recreational and forest resources of southwestern Oregon will be emphasized, and an opportunity to observe them will be provided by a field trip June 27-July 5 along the Oregon coast, to Crater Lake, and through the Redwood country. For additional information write to the college Department of Natural Resources.

The **Scientific Research Society of America** installed its fourteenth branch at the Du Pont Experimental Station Jan. 29. Two hundred charter members participated in the program, at which Detlev W. Bronk, AAAS president, gave the principal address. John T. Maynard was elected president, Raymond L. McCarthy vice president, John M. Griffing secretary, and Northrop Brown treasurer.

William B. Fox, of North Carolina State College, has been elected president of the **Southern Appalachian Botanical Club**, succeeding Royal E. Shanks. Wilbur H. Duncan was elected vice president, Nelle Ammons treasurer, and Elizabeth Ann Bartholomew secretary.

Miscellaneous

The **USDA Bureau of Animal Industry** is transferring its section conducting beef-cattle investigations from Beltsville, Md., to Denver, which will facilitate coordination of projects already under way at five other field stations. A. L. Baker is being transferred to Denver from the Front Royal (Va.) Beef Cattle Research Station to assist R. T. Clark, head of the section since 1949. His place as head of the Front Royal Station will be taken by Robert M. Priode.

Certain technical files of the **U. S. Geological Survey's Paleontology and Stratigraphy Branch** have been released as Open File Reports, and arrangements have been made whereby either microfilm or paper facsimile copies may be purchased at cost of reproduc-

tion. The Map Information Office of the Survey, Washington 25, D. C., will furnish further information.

The **Alexander C. Humphreys Foundation**, organized last year to honor the memory of the second president of Stevens Institute of Technology, has elected Alan Hazeltine, electronics consultant and Stevens faculty member, president. Other officers elected were: vice presidents, Henry B. Cross, Robert F. Jacobus, and Frederick M. Gibson; secretary, H. Sherman Loud, Jr.; and treasurer, Richard A. Wolff. Bernard D. Klein, outgoing president, was elected honorary president.

The **Institute of Metals**, London, has made the following awards for 1952: The Institute of Metals Medal to William S. Robinson, for his services to the nonferrous metal industries in developing the Australian zinc-lead and the British zinc industry; the Rosenhain Medal to André Guinier, Conservatoire national des arts et métiers, Paris, for outstanding contributions in the field of physical metallurgy; and the W. H. A. Robertson Medal to Cyril E. Davies, for his paper on "The Cold-Rolling of Non-Ferrous Metals in Sheet and Strip Form."

A **National Anti-Cancer League** has been formed in Sweden with the objective of supporting scientific research on cancer, a disease that annually takes a death toll of 12,000 persons in Sweden. The new association will have low membership fees, thus enabling a large proportion of the population to participate.

The **Ohio Journal of Science** is offering a cash prize for the outstanding paper in the field of chemistry, either unpublished, or published in the *Journal* after July 1, 1951. The contestant must be a member of the Chemistry Section of the Ohio Academy of Science, and the manuscript must be based upon original research. Further information may be obtained from the editor, Ohio State University, Columbus.

Chemicals wanted by the **Registry of Rare Chemicals**, 35 W. 33rd St., Chicago 16, include: potassium sodium cobaltinitrite; ammonium dithionate; beryllium phthalocyanine; triisopropyl phosphate; 2,3-benz-9-anthrone; benzyl isonitrile; 1,4-dihydroxy-5,8-dichloroanthraquinone; dimethylaminoethyl carbamate; 2,2-dimethylpentanone-4; 3-ethyl-2-aminophenyl benzthiazoline; 2-hydroxynaphthalene-8-sulfonic acid; 2-methyloxazole; 1,3,6-trihydroxynaphthalene; *m*-tyramine; thymine-2-desoxyriboside; *p*-hydroxyphenyl serine; ferrous albuminate; avidin; coprostanone; and 3,5'-diiodothyronine.

The proceedings of the **Second Alaskan Science Conference**, held in September at Mount McKinley National Park under the auspices of the AAAS Alaska Division, is a 175,000-word volume containing more than 80 reports of studies in 20 scientific fields. A limited number of copies are available for distribution outside the territory. The price is \$2.00, and requests should be addressed to the Editorial Committee, Box 50, Juneau, Alaska.

Technical Papers

Some Applications of the Rapid Uptake of Vitamin B₁₂ by Resting *Lactobacillus leichmannii* Organisms

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In our previous paper (1), it was demonstrated that certain microorganisms such as *Lactobacillus leichmannii* (ATCC 4797) incorporated the radioactivity of exogenous vitamin B₁₂ tagged with Co⁶⁰ in the growing cells, whereas organisms like *L. arabinosus* did not. Experimental evidence indicated that the radioactivity was due to vitamin B₁₂ per se and not to any simple Co⁶⁰ compounds. This study has been extended to follow the uptake of vitamin B₁₂ by "resting" bacterial cells. The results are reported here.

Quantitative uptake of vitamin B₁₂ by "resting" cells. Two hundred ml of Skeggs and Wright (2) medium, to which was added a total of approximately 10 µg crystalline vitamin B₁₂, was inoculated with *L. leichmannii* and incubated at 37° for 43 hr. This concentration of vitamin B₁₂ in media (i.e., 0.5 µg/10 cc) represented approximately one half the amount supporting the maximum growth of *L. leichmannii*, according to our data on dose-growth response curve. The organisms were harvested by centrifugation, washed once with 25 ml 0.85% saline solution, and resuspended in sufficient (approximately 40 ml) salt solution to give a turbidity reading of 400 in a Klett-Summerson photoelectric colorimeter with #42 filter. This suspension was used for subsequent studies on the quantitative absorption of vitamin B₁₂ in test solutions.

One ml of the bacterial suspension was added to 20 ml 0.85% NaCl solutions containing measured amounts of radioactive vitamin B₁₂. The mixture was allowed to stand at room temperature for 30 min or less, with intermittent shaking, and then centrifuged at 1500 rpm for 15 min. The supernatant fluid was sucked off through a capillary tube, and the packed organisms were transferred quantitatively to a planchet. Radioactivity was measured with a Geiger-Müller thin mica window counter.

The results of a typical recovery experiment are given in Table 1. They demonstrate that the recovery was quantitative over an approximately 64-fold range between 0.5 to 32 µg or more. With larger quantities of the organisms, the amount of vitamin B₁₂ recovered could be increased proportionately. Even smaller

¹The authors acknowledge grants-in-aid from Sharp & Dohme, Inc., The Squibb Institute for Medical Research, Upjohn Company, Merck & Co., Inc., and The National Vitamin Foundation.

TABLE 1
RECOVERY OF VITAMIN B₁₂ FROM RESTING
CELLS OF *L. leichmannii*

Radioactive vitamin B ₁₂ added (µg)	Radioactivity in washed cells (measured as µg radioactive vitamin)	Recovery in cells (%)
0.5	0.5	100
1.0	1.0	100
2.0	2.0	100
4.0	4.0	100
8.0	8.0	100
16.0	16.0	100
32.0	32.0	100
64.0	55.0	85
128.0	96.0	55
256.0	126.0	50

amounts of radioactive vitamin B₁₂ could be measured with equal accuracy if a more sensitive counter were employed. No self-absorption corrections were made, since the solid content per sq cm of the planchet was found to be on the order of 3 mg/cm² or less.

Effects of pH and salt concentrations. Attempts were made to ascertain the effect of pH and of salt concentrations on the recovery of radioactive vitamin B₁₂. To this end, 2.0-ml aliquots of radioactive vitamin B₁₂ solution (10 µg/ml) were added to 20-ml portions of Skeggs and Wright medium previously adjusted (with N/1 HCl or N/10 NaOH) to various pH's, ranging from 2 to 9, and to 20-ml portions of NaCl solutions of different concentrations ranging from 0.2 to 4.3%. In these adjustments of pH no effort was made to keep the ionic strength constant. One ml of a suspension of *L. leichmannii* was again added to each solution and allowed to stand at room temperature for 30 min. The radioactivity in different samples was measured according to the procedure described above. Recovery was essentially complete between pH 3 and pH 9. At higher pH's recovery was greatly reduced. For example, at pH 10 only 10% of the added radioactivity was found in the cells.

In the pH range of unbuffered NaCl solutions the recovery was markedly affected by salt concentra-

TABLE 2
EFFECT OF NaCl CONCENTRATION ON UPTAKE OF
RADIOACTIVITY OF VITAMIN B₁₂

Salt concentration (%)	Recovery (%)
0.2-1.4	90-100
1.7	85
2.2	65
2.6	45
3.4	12
4.3	10

tions, being practically quantitative at low salt concentrations, and progressively poorer at higher concentrations. For example, in 1.7% NaCl solution (i.e., twice isotonicity) recovery was only 85% (Table 2).

These results demonstrate that under appropriate conditions it is possible by these techniques to separate quantitatively the vitamin B₁₂ from dilute solutions. If the vitamin B₁₂ to be assayed contains Co⁶⁰, radioactivity in the cells may be taken as a measure of the vitamin content. This method is ideally suited to the estimation of radioactive vitamin B₁₂ in the urine of rats given small subcutaneous injections. In this situation the samples could not be assayed satisfactorily by the usual microbiological method, both because of the low activity and because of the presence of inhibitors that prevented the use of larger aliquots. Approximate measurements could be made if the vitamin were separated by repeated extraction with normal butanol after the addition of solid ammonium sulfate to the specimens, and the radioactivity in the butanol determined. Results of determinations following both *L. leichmannii* uptake and the butanol extraction of radioactivity in urine collected 24 hr after subcutaneous injection of 1.0 µg of Co⁶⁰ tagged vitamin B₁₂ are compared in Table 3.

TABLE 3
DETERMINATION OF RADIOACTIVE VITAMIN B₁₂
IN RAT URINE

Samples	Method employed*	
	Uptake by resting cells	Butanol extraction
Normal rat urine + 5 µg vitamin B ₁₂	4.2	3.5
Normal rat urine + 20 µg vitamin B ₁₂	18.5	14.0
Normal rat urine + 40 µg vitamin B ₁₂	37.0	26.0
Urine (A)†	9.0	6.0
Urine (B)†	12.0	7.8
Urine (C)†	13.6	10.2

* The radioactive vitamin B₁₂ recovered by each method was expressed as µg/sample (20 ml). One µg was found to give 10 cpm.

† The samples of urine were obtained from adult rats 24 hr after injection of 1 µg radioactive vitamin B₁₂.

They demonstrate that the activity obtained by the method of absorption on microorganisms yielded consistently higher results than the extraction method. The higher values are probably more nearly correct, since control recovery experiments in which known amounts of radioactive vitamin B₁₂ were added to normal urine gave more nearly quantitative results by the *L. leichmannii* uptake method.

The rapid and quantitative isolation from solution of vitamin B₁₂ by microorganisms such as *L. leichmannii* also lends itself to assay of nonradioactive vitamin B₁₂. This has been accomplished either by the isotope dilution technique (i.e., by adding a known amount of radioactive vitamin B₁₂ to the test solution followed by subsequent addition of a standardized

suspension of organisms with uptake of a definite amount of vitamin B₁₂) or by microbiological determination of vitamin B₁₂ in the cell mass. In the latter case, after centrifugation and washing, if the cells are suspended in normal saline solution and killed by heating at 60° for 1 hr, the vitamin B₁₂ in the cell mass is available to the test organisms used in the assay method of Skeggs and Wright. The main advantage of our procedure lies in concentrating the small quantities of vitamin B₁₂ by the use of bacteria. The details of these methods and further applications will be published elsewhere.

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On the Interaction of Mesons and Plural vs. Multiple Meson Production

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Recent experimental work by Bernardini *et al.* may throw some light on the nature of the interaction of π -mesons with nucleons as well as suggest a new interpretation of the problem of multiple vs. plural meson production. It is well known that the question of multiple vs. plural meson production may be in good part an outgrowth of our lack of knowledge concerning the nature of nuclear forces and the elementary interaction process (1).

Bernardini, Booth, and Lederman (2) have found that the very strong inelastic nuclear scattering of negative π -mesons in which the energy losses exceed 50%, as well as the negative π -meson nuclear absorption involving catastrophic processes, are strongly energy-dependent and occur only for energies greater than about 60 mev. The frequency of these anomalous scatterings, as well as the existence of cases showing energy losses close to 100%, casts doubt on the validity of the free nuclear model of the nucleus (3). The possibility of explaining the observations in terms of multiple elastic collisions inside the nucleus, instead of the single π -nucleon collisions, is also unlikely in view of the recent results of Chedester *et al.* (4). In a personal communication Bernardini has informed the writer that there is some direct evidence that this type of anomalous scattering could be interpreted as an interaction of a negative π -meson with a group of nucleons (containing 3 or 4 nucleons) acting as a whole. The scattering experiments cited above suggest the excitation of such nuclear groups or subunits of the nucleus, and may indicate the operation of a many-body type process. The experimental results also lend themselves to an interpretation which suggests that the anomalous scattering of π -mesons of energies greater than about 60 mev by complex nuclei

may be a function of the density of the nucleons in a volume of the order involving the Compton wavelength of the meson.

There is other recent evidence of the failure of conventional interactions and models. In particular, one may cite the work of Chamberlain, Segrè, and Wiegand (5) on p - p scattering from 120 to 345 mev. These authors have found that all theoretical investigations so far, based on static potentials, including the work of Christian, Jastrow, and others, have failed to explain their experimental results. Thus, the experimental evidence of both Bernardini *et al.* and Chamberlain *et al.* points to the possible operation of nonlocalizable, velocity-dependent forces of the many-body type.

Osborne (6) has presented experimental evidence of pluromultiple meson production in high-energy cosmic-ray showers. He points out that, although the events in light nuclei are not inconsistent with a single collision model, the heavier nuclei events cannot be described by this model. In view of the probable nature of nuclear forces as indicated by the evidence from the scattering experiments cited above, it is the author's opinion that the simple picture of pure plural meson production by individual nucleon-nucleon encounters is quite likely not valid. What in the past have been taken for examples of pure plural meson production in cosmic-ray showers by individual nucleon-nucleon encounters probably involve multiple production in one single act by nucleons acting as nuclear subunits or groups. These groups of nucleons may be those outside the nuclear core, which is consistent with evidence presented by R. F. Mozley (7) and R. D. Miller (8) on photonuclear stars, which indicates that only the surface nucleons are effective in producing π -mesons. In the phenomenon of pluromultiple production there may be more than one such group involved. Although it is not unlikely that there may be no such phenomenon as pure plural meson production, there seem to be two types of multiple meson production: the type ordinarily encountered involving nucleonic groups and the type first observed by Lord, Fainberg, and Schein (9), wherein the nucleonic volume involved in these extremely high-energy interactions is so small as to preclude the presence of groups of nucleons, but nevertheless may be the site of the excitation of the nucleon-antinucleon field, the heavy nuclear quanta fields (embracing mesons of the τ and V type) and the surrounding pion field.

The volumes of interaction discussed above suggesting the nonlocalizability of nucleonic interactions may be termed "elementary volumes" and may be identified as functions of the elementary lengths. Thus, there is more than one elementary length, and in this context they may be interpreted as not so much imposing limitations to the behavior of natural phenomena as the natural constants c , e , and \hbar do, but rather as serving to define the application of various physical models and concepts. For instance, in the experiments of Bernardini *et al.* the elemen-

tary length involved (the mesonic Compton wavelength) limits the application of the free nucleon model of the nucleus, as well as the concept of the static potential (10). On the other hand, the elementary length (probably the protonic Compton wavelength) involved in the phenomenon of the multiple production of particles involving single nucleon volumes may limit, if one is permitted to speculate, the unambiguous application of the elementary concepts of particle and field.

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A Rapid Titrimetric Method for Determining the Water Content of Animal Tissues¹

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The most widely used method for determining the water content of animal tissues is that whereby the material is dried to a constant weight in an oven. This method is subject to certain disadvantages, notably the danger of decomposing some of the complex organic compounds if too high a temperature is employed and the time consumed in drying and weighing. These difficulties are to a great extent obviated by the use of the Karl Fischer reagent and the titrimetric estimation of water.

This procedure is fully described in the recent book by Mitchell and Smith (1) and has been widely utilized in industrial laboratories for the determination of the water content of many substances such as paper, reagents, and foodstuffs. We have encountered no record of its adoption by physiologists and biochemists, but we believe that it would prove of considerable value to these investigators.

For determining the water content of blood we first weigh a capillary tube approximately $\frac{1}{2}$ in. in length.

¹This investigation was carried out under contract N7onr29544 between the Office of Naval Research and the University of California.

²Lt., USNR, Office of Naval Research Unit No. 1, University of California, Berkeley. The opinions contained herein are the private ones of the writer and are not to be construed as official or reflecting the views of the Navy Department or the Naval service at large.

Having nicked the tail of a rat so as to expose a small drop of blood, the latter is touched with the end of the tube, which then fills by capillarity. The tube holding the blood is again weighed and dropped into a 100-ml glass-stoppered volumetric flask containing about 20 ml of a mixture of the Fischer reagent and methyl alcohol. This mixture has previously been brought to a light cherry color so as to match a color standard. The capillary tube is cracked open while in the reagent by tapping with a glass rod. The water decolorizes the Fischer reagent, and this is back-titrated with more reagent to the original color. The operation takes about 3 min and the end point is definite.

The preparation of solid material is likewise simple. A small piece of tissue (muscle, liver, brain) weighing from 100 to 250 mg is excised and placed upon a tared slip of filter paper. After rapid weighing the paper and tissue both are dropped into the flask containing the reagent. In order to facilitate the extraction of the water, the tissue mass is crushed with a glass rod. Titration then follows. A blank for the water in the filter paper is secured by extracting and titrating a plain piece equal in weight to that used in the experiment.

In order to test the method we examined both whole blood and tissues of normal adult laboratory rats. Samples of blood were taken from 55 rats and titrated with the Fischer reagent. The values for water showed a range of 77-80%, with a mean of approximately 79%, values which correspond very closely to those found by numerous previous investigators who used the standard drying methods.

For tissues we used muscle, liver, and brain. Three rats were sacrificed. From each we took two samples of the tissues mentioned. The water content of one sample of each pair was determined by the titration method. That of the other sample was determined by placing the tissue in an oven at 90° C and drying to constant weight. For the three rats the results were as shown in Table 1, expressed as percent of water.

TABLE 1

Tissue	Percentage water found by	
	Titration	Drying
Muscle	74.1	74.4
	74.1	74.7
	74.6	74.6
Liver	72.1	72.1
	73.2	74.2
	72.4	72.6
Brain	79.2	78.3
	77.1	77.5
	79.1	76.3

The slight variation in estimate of water content found by the two methods appears to be purely random in character. Their accuracy therefore is substantially equal. The advantage of the titrimetric method lies in the rapidity with which the determinations may

be made. With it one may not only secure immediately the data pertaining to an extensive array of samples but he may also follow changes in the water content of blood or tissue almost as soon as they occur. The procedure thus lends itself particularly neatly to periodic blood tests or biopsies performed with laboratory animals or even man.

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Bone Implantation as a Means of Studying Vitamin D Action^{1,2}

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The specific action of vitamin D in the body economy is still to be determined; in fact, there is still no agreement as to the locale of its action. In 1924 Shipley (1) demonstrated calcification *in vitro*, using non-rachitic serum as a calcifying medium. Fischmann (2) noted that rachitic serum would not calcify osteogenic tissue and failed to compensate for the deficiency by addition of calcium and phosphorus. This suggests the possibility that healing of rickets is dependent on the presence of vitamin D or some derivative thereof. Sobel and co-workers (3), however, showed that calcification took place *in vitro* without the presence of vitamin D.

It would appear as a result of these excellent *in vitro* investigations that vitamin D exerts its influence on the environment from which bone receives its mineral. An attempt to test the above observations with *in vivo* studies was carried out by using the intact animal as the culture medium.³

Tibiae were taken from 1-day-old chicks, and one of each pair was placed under the skin of a 2-week-old rachitic or nonrachitic chick. The bone was inserted alongside the ribs through a small incision, which was immediately sewn up. The host chicks were fed AOAC rachitogenic diet without vitamin D or with 1 unit vitamin D/g of feed throughout the experiment.

After 4 days the implanted tibia was removed and the Ca content compared with that of its nonimplanted mate. The results are shown in Table 1. In the rachitic host the bone lost calcium, whereas in the nonrachitic host a slight amount was gained, indicating the presence of a pathological change in the composition of the body fluid of a rachitic animal.

It should be noted that the loss or gain of Ca shown in Table 1 is the resultant of the amount of Ca that entered and the amount that left the bone through ex-

¹ Presented at the Congress of the International Union of Pure and Applied Chemistry, New York 1951.

² Contribution No. 214 of Division of Chemistry, Science Service.

³ The assistance of L. J. Carter and P. M. Richard with the care and treatment of the animals is gratefully acknowledged.

TABLE 1
CALCIUM CONTENT OF PAIRED CHICK BONES
BEFORE AND AFTER IMPLANTATION

Rachitic host			Nonrachitic host			
Left tibia (mg Ca)	Im- planted right tibia (mg Ca)	Ratio	Left tibia (mg Ca)	Im- planted right tibia (mg Ca)	Ratio	
7.80	6.70	.86	7.85	8.12	1.03	
8.05	7.72	.96	8.90	9.45	1.06	
7.38	6.30	.85	7.55	7.40	1.01	
7.00	6.50	.86	6.80	6.85	1.01	
7.82	7.05	.90	7.52	7.38	.98	
9.05	8.10	.90	7.30	8.20	1.12	
Mean	7.95	7.06	.89	7.62	7.90	1.04

change, deposition, and solution. An attempt was made to approximate these separate quantities by implanting a bone made radioactive with Ca^{45} . In this experiment 12-day-old rachitic and nonrachitic chicks were made radioactive by injection of $1 \mu\text{e Ca}^{45}$. The chicks were killed 48 hr later, and both tibiae removed. One was kept for reference, and the other was implanted, as above, into a 3-week-old rachitic or nonrachitic chick. Seven days later the implanted tibiae were removed, and their content of Ca and Ca^{45} was compared with their nonimplanted mates. The Ca^{45} analyses were carried out according to the method described by Migicovsky and Emslie (4).

The summarized results are shown in Table 2. It is seen that the loss and the gain of Ca in the non-

TABLE 2
EFFECT OF RACHITIC STATE ON MOVEMENT OF
CALCIUM IN IMPLANTED CHICK TIBIAE

Mean (8 values)	Implanted normal bone		Implanted rachitic bone	
	Normal host	Rachitic host	Normal host	Rachitic host
Net difference* mg Ca	0.48	-2.80	1.62	-2.76
Total loss† mg Ca	4.51	9.61	3.85	8.64
Total gain‡ mg Ca	4.99	6.81	5.47	5.88
Ratio§	0.90	1.40	0.67	1.46

* Mg Ca/implanted tibia - mg Ca/nonimplanted tibia.

† Cpm of nonimplanted tibia - cpm of implanted tibia.

Mean specific activity of implanted and nonimplanted tibia.

‡ Net difference plus total loss.

§ Total loss

§ Total gain

rachitic host were less than in the rachitic host, and the ratio of loss to gain was less in the nonrachitic host.

A similar experiment was conducted with rachitic and nonrachitic rats, except that nonrachitic femurs were implanted into the peritoneal cavity. The summarized results are shown in Table 3.

This technique of using the intact animal as the culture medium for a bone from another animal has

TABLE 3
EFFECT OF RACHITIC STATE ON MOVEMENT OF
CALCIUM IN IMPLANTED RAT FEMORA*

Mean (4 values)	Implanted normal bone	
	Normal host	Rachitic host
Net difference mg Ca	1.21	0.46
Total loss mg Ca	1.16	3.65
Total gain mg Ca	2.36	4.31
Ratio	.48	.84

* Calculations as in Table 2.

demonstrated that in rickets the changes in the composition of body fluid could be the cause of the rachitic lesions of bone. These lesions could arise by virtue of an increased rate of Ca solution relative to the rate of Ca deposition. The problem of how vitamin D prevents the changes in the body fluid remains to be resolved, although there is strong evidence favoring the absorption mechanism.

In addition it has been observed that after 7 days the ends of the implanted bone became encapsulated by a cellular tissue which was partially calcified. A similar observation had been made by Bull (5) with rabbit bone fragments implanted into abdominal muscle.

It appears that this cellular tissue and the implantation technique herein described could be advantageously employed in the study of the calcification mechanism. Further study along this line is in progress.

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The Critical Frequency of Taste

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One of the classical experiments in the field of gustation is a study reported in 1925 by Allen and Weinberg (1), which presents rather unequivocal evidence for four taste systems and their relative sensitivities, based upon the fusion frequency of electrical stimuli applied to the tongue. In the discussion of gustation in a recent important handbook (2) these results have been cited in some detail, and considerable weight has been given them. The present authors, however, encountered considerable difficulty in following Allen and Weinberg's reasoning and statistical procedures, and, in the absence of the raw data,

measures of variability, and results from more than a single subject, decided that the experiment would bear repetition.

Two attempts were made to duplicate the results. In the first attempt a Goodwin Stimulator (Model No. 3) was used, which delivered an exponential discharge with an abrupt rise time and a time constant of 0.5 σ . The active electrode was a small piece of tantalum wire, doubled and drawn to a point. The inactive electrode was a small coil of tantalum wire which rested under the tongue. The anterior dorsal surface of the tongue was explored with stimuli of 0.4–3.0 v at frequencies of 100–1000 cps. Below 0.8 v no sensations were aroused, but at 0.8 v all frequencies aroused pressure or cold sensations. Sour was not in evidence until 0.9 v was reached and then was accompanied by cutaneous sensations. Sour sensations, when obtained, were either continuous or accompanied by pressure or pain which sometimes fluctuated. It would have been easy to confuse continuous sour plus discrete pressure pulses with discrete sour pulses. Similar results were obtained with a second trained subject. It was concluded that the judgment required of the subject was too difficult to permit of precise results. The first apparatus was abandoned as being unfair to Allen and Weinberg, and a second apparatus was assembled which was designed to deliver a stimulus resembling more closely the stimulus used by them.

Allen and Weinberg used mechanical control of the stimulus, whereas the present authors attempted to duplicate the essential features of their stimulus using electronic control. An audio-oscillator (Hewlett-Packard Model 200B), a square-wave generator (Hewlett-Packard Model 210A), and an attenuator (Hewlett-Packard Model 350A) were employed to deliver half a square wave, variable as to voltage and frequency. The active electrode (the cathode, as in Allen and Weinberg's study) was the same as in the first study; the inactive electrode was a double strand of tantalum wire stretched across a plastic plate on which the subject rested his tongue. A silver active electrode (similar to Allen and Weinberg's) was used in some series, with no change in results.

In the second study six subjects were used, of whom four were experienced in psychophysical judgments. They were instructed to report any and all sensations and to describe the time characteristics of any sensations experienced. As before, the anterior dorsal surface of the tongue was explored with stimuli of increasing voltage until sour was aroused. Experimentation began with 0.11 v, and the stimulus never exceeded 2.08 v. Then the frequency of the stimulus was varied from 20 to 300 cps. All subjects reported sour, seldom accompanied by other sensations, so that it was possible to observe the time course of the sour sensation. In no instance did any subject spontaneously report fluctuating or pulsing sour. When finally queried as to whether discrete pulses of sour occurred, no subject was able to observe it. For all subjects, then, sour was "fused" at

all frequencies, and it thus became impossible to obtain fusion frequencies, as reported by Allen and Weinberg.

The reasons for the discrepancy in results are not obvious. It is possible that Allen and Weinberg's subject was confused by cutaneous sensations aroused simultaneously with sour. In any event, unless their results can be substantiated by other investigators, they should not be used as evidence for four taste systems nor for the relationships among the taste systems.

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Skeletal Units in Protein Crystals¹

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Recent estimates of the numbers of amino acid residues in various protein structures are of interest in relation to the idea that the manner in which the amino acid backbones polymerize to form the skeletons of native protein molecules may be characteristic for proteins as such (differentiating proteins from amino acid polycondensations which are not proteins) and that there may be a single skeletal type in all the individual chemical entities of proteins or a homologous series of types embodying some common constructional principle (1). For horse hemoglobin, ~580 residues are estimated (2), 6 with free α -amino groups (3); for horse (2) and whale (4) myoglobin, 146 and ~147 residues are suggested, one of each set having a free α -amino group (3, 4). For ribonuclease, a complement of 100 ± 10 is proposed (5); for the trigonal insulin structure (6), three substructures, each with ~102 residues (7) (4 with free α -amino groups [8]) are diagnosed (9).

From these figures there arises the possibility of a single type of skeleton in which about 48 residues are interlocked, with or without additional residues inserted by a single terminal and acting as substituents. (The fact that such a skeleton presents itself in the cyclol system [10] will be discussed elsewhere.) The ribonuclease structure would have 2 such units, the myoglobins 3, and insulin three sets of 2 such units. For horse hemoglobin (and probably also for the many other hemoglobins with about the same mol wt) the number would be 12.

Studying the idea of a characteristic skeleton or skeletons first in the form of the postulate of a single molecular skeleton for proteins in general, we see that the description of a protein structure would

¹ This work is supported by the ONR under contract N8onr-579.

have 3 elements (11): (1) the number of the individual skeletons; (2) the arrangement in space of the skeletons—i.e., the molecular pattern of the structure; (3) specifications of the manner in which the various complements of R_1, R_2, \dots side chains are inserted into the sites of each skeleton. If this situation materializes, there may well be general principles regarding the sets of points with which the skeletons—and also water clusters—are associated (11). Molecular and water cluster patterns associated with points of cristobalite and tridymite networks, for example, would explain many facts regarding the space groups of crystalline proteins and the nature of various protein intergrowths (12). We also notice that a supposed difficulty (2) in the relation between, for example, the myoglobin and the hemoglobin of horse is resolved in this system of ideas. The myoglobin is, seemingly, not a precursor of the hemoglobin: how, then, can an apparent structural relation between them be explained? The difficulty disappears when we see that the myoglobin would have a certain system of skeletons characteristically substituted, and the hemoglobin the same set four times repeated, also characteristically but differently substituted.

In the light of these results, the time seems ripe for the application to intensity maps of protein crystals, as they become available, of certain of the techniques prepared for this purpose (13). It has been shown that a structure comprising a unit D repeated by translation at a set of points has the transform $T = T_D T_D$. In such a case we may make tentative assumptions regarding δ and D and construct new intensity maps entry by entry, the map $|T|^2/|T_D|^2$ when D is "given," the map $|T|^2/|T_D|^2$ when δ is "given." The transform of the first is, then, the vector map of the molecular pattern; the transform of the second is the vector map of the unit D . The transforms of a variety of structural types and of various kinds of molecular pattern, which have already been recorded (13), may prove useful in this connection. With the present viewpoint, the shapes of protein structures (such as the hemoglobin structure with mol wt $\sim 66,700$) are functions of all three elements cited above. From these shapes the shape of the unit is not deducible. A possible starting point, however, is the assumption of a globulite type of skeleton, in which there is no gross difference in dimensions in various directions. The testing of this hypothesis from intensity maps of protein crystals is in progress.

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An Inhibitor of Desoxyribonuclease in Human White Blood Cells and Bone Marrow Cells and its Relationship to Cellular Maturity¹

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Inhibitors of the enzyme desoxyribonuclease (DNase) have been reported. Zamenhof and Chargaff (1) have noted an inhibitor in yeast that is specific for yeast DNase. Laskowski *et al.* (2) have reported a similar, but not identical, inhibitor in the crop gland of the pigeon; and, in another communication (3), an inhibitor in various normal and cancerous tissues (human), as well as in the tissues of the normal rat, has been noted. No significant variations in the amount of inhibitor per gram weight of tissue were demonstrated. No studies have been reported on human blood or bone marrow cells, with the exception of one human marrow (3).

In the present work, the DNase inhibitor content of human white blood cells and bone marrow cells, both from normal subjects and from patients with leukemia, was determined. It was found that the inhibitor activity present in the cells varies with the degree of cellular immaturity. The inhibitor activity of mature human white blood cells averaged 37.4%/10⁴ cells. The inhibitor activity of the primitive blast cells from acute leukemia was close to zero. Cells of intermediate degrees of maturity were found to have intermediate amounts of inhibitor.

A viscosity method was used for the determination of the enzyme inhibitor. The DNase activity was measured by the time required for the enzyme to reduce to one half the relative viscosity of a solution of desoxyribonucleic acid (DNA). The inhibitor activity of a given cell extract was measured by the amount of enzyme inactivated and is expressed as the percentage of the enzyme inactivated by the extract of 10⁴ cells. Cell extracts of whole blood and of bone marrow were prepared by dilution (1/100) with water. The inhibitory activity of whole blood was found to reside solely in the white blood cells. Neither hemolyzed red cells nor plasma had appreciable inhibitor activity. The technique is to be described elsewhere (4).

The concentration of the desoxyribonuclease inhibitor in the various types of cell preparations is summarized in Table 1. The normal mature poly-

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TABLE 1
VARIATION IN THE DN-ASE INHIBITOR ACTIVITY WITH
CELL TYPE IN VARIOUS DISEASES

Tissue	Principal cell types (%)						
	Inhibition/ ^a cells (%)	Polymorphonuclear leucocytes	Lymphocytes	Metamyelocytes	Myelocytes	Pro-myelocytes	Myeloblasts Normoblasts
Normal blood	37.4	59	39				
Lymphosarcoma and Hodgkin's, blood	32.4	62	38				
Chronic myelocytic leukemia, blood	31.9*	74	16	3	2	1	
	10.8†	27	0	17	32	21	4 23
Normal bone marrow	14.3	46		13	9	2	
Lymphosarcoma and Hodgkin's, marrow	14.8	44		13	21	1	1 15
Chronic myelocytic leukemia, marrow	6.8	35		12	31	11	8 3
Acute myelocytic leukemia, blood	4.2	16	3	5	4	71	
Acute myelocytic leukemia, marrow	2.7	11		4	13	27	42
Chronic lymphocytic leukemia, blood	12.1	11	88				
Chronic lymphocytic leukemia, marrow	8.1	10	83	1	1		
Acute lymphocytic leukemia, blood	0‡	3	97 (and/or blasts)				
Acute lymphocytic leukemia, marrow	0‡	0	100 (and/or blasts)				

* Chronic myelocytic leukemia under treatment.

† Chronic myelocytic leukemia in relapse.

‡ Excess enzyme present.

morphonuclear leucocytes and lymphocytes of the blood contain the highest concentration of inhibitor—namely, 37.4%/10⁴ cells. Extracts of the less mature cells from the normal marrow exhibit a concentration of one third this value.

Consistent with these findings, the blood and marrow from patients with lymphosarcoma and Hodgkin's disease which are morphologically normal have normal quantities of inhibitor activity.

The more primitive cells of the blood and marrow from leukemic patients show inhibitor activities between 12.1% and 0% per 10⁴ cells. In chronic myelocytic leukemia, when, as a consequence of treatment, the peripheral blood cells were qualitatively normal, the inhibitor content was 31.9%. In contrast, the inhibitor activity of the more immature blood cells of leukemic patients in relapse averaged 10.8%/10⁴ cells. These data indicate that the absence of inhibitor is not a manifestation of malignancy per se. The progressive decrease in inhibitor activity is paralleled by an increase in the number and degree of immaturity of the cells (and a decrease in the number of mature cells) from which the extracts were prepared. This suggests that a close relationship exists between the degree of immaturity of the cells studied and their content of DN-ase inhibitor.

The existence of DNA in a highly polymerized

form in the cell nucleus and particularly in the chromosomal apparatus is well known. Its synthesis and degradation, therefore, must be of prime importance in cellular division and growth. DN-ase, an enzyme capable of depolymerizing DNA, has been detected in many tissues and is probably a constituent of all cells. Highly polymerized DNA is resistant to the action of phosphatases, but may be easily split after depolymerization by DN-ase.

The presence of an inhibitor of DN-ase in cells indicates a possible regulatory mechanism to control the breakdown of DNA. The association of DNA with the chromosomes and hence with cell division, and the present demonstration of a correlation between the inhibitor content and cell maturity, suggest that the inhibitor is intimately associated with the control of cell division and multiplication. Complete data covering the above studies are to be reported (5).

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Action of Chymotrypsin α and Chymotrypsin B upon Several Protein Substrates¹

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It is well known that native proteins are more resistant to proteolytic digestion than denatured proteins. The generally accepted explanation is that this is due to the protective arrangements of the non-specific groups on the molecule of the substrate. An attempt was made to investigate a reversed case—namely, the influence of the nonspecific groups of the enzyme molecule on the rate of proteolytic digestion. Crystalline chymotrypsin α (1) and crystalline chymotrypsin B (2) were used. Both enzymes are known to have identical specificity toward synthetic substrates (3) but different isoelectric points (4). Although it has previously been shown that chymotrypsin B digests casein with a somewhat slower rate than chymotrypsin α (5), it was interesting to ascertain whether this difference in the rate of digestion persists with other protein substrates.

The following crystalline proteins were prepared and used as substrates: egg albumin (6), edestin (6),

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² Some of the data included in this report were taken from a thesis submitted by John A. Ambrose to the Graduate School of Marquette University in partial fulfillment of the requirements for the M.Sc. degree. Present address: Department of Chemistry, Oregon State College, Corvallis.

TABLE 1*

Substrate	Percentage
Egg albumin, heat-denatured	46
Egg albumin, urea-denatured	75
Edestin, heat-denatured	86
Edestin, urea-denatured	79
Chymotrypsinogen α , undenatured	48
Hemoglobin, urea-denatured	91
Lysozyme, " "	101

* Figures indicate percentage of digestion by chymotrypsin B, when digestion by chymotrypsin α is 100.

chymotrypsinogen α (1), dog hemoglobin (7) and lysozyme (8). In order to secure a faster rate of reaction some of the substrates were denatured either by heating (30 min at 100° C) or by urea (9). The insoluble precipitate was centrifuged off and discarded, and the soluble portion was used. The concentration of substrate was expressed in optical density at 280 m μ and in most cases was adjusted to E_{280} = 3.0. The proteolytic activity was determined spectrophotometrically according to Kunitz (10).

The results of experiments with different substrates at pH 7.6 are shown in Table 1. Digestion by chymo-

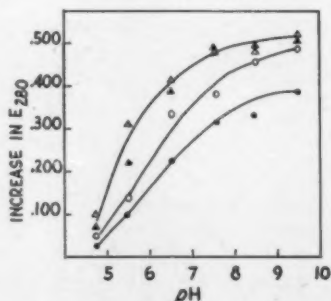


FIG. 1. —○—, Chymotrypsin α , urea-denatured egg albumin; —●—, Chymotrypsin B, urea-denatured egg albumin. —△—, Chymotrypsin α , urea-denatured lysozyme; —▲—, Chymotrypsin B, urea-denatured lysozyme. 500 γ of enzyme and the concentration of substrate E_{280} = 3.0 in all tubes. Incubation time, 20 min. All figures corrected for blanks. Buffers 4.5 and 5.5 acetate, 6.5 and 7.6 phosphate, 8.5 and 9.5 borate.

trypsin α was faster than by chymotrypsin B except in the case of urea-denatured lysozyme, in which both enzymes gave the same results. The observed differences in the rate of digestion by the two chymotrypsins persisted through a fairly wide range of pH values, as shown in Fig. 1. Confirming previous re-

TABLE 2

END POINTS OF DIGESTION BY THE TWO CHYMOTRYPSINS

Substrate*	Chymotrypsin α E_{280}	Chymotrypsin B E_{280}
Egg albumin, urea-denatured	0.660	0.606
Hemoglobin, " "	.473	.492
Lysozyme, " "	.643	.650
Lysozyme, native, fresh	0.495	0.157

* Concentration of substrates adjusted to give the value of E_{280} = 3.0, 1000 γ of enzyme, incubation 3 hr, at 37° C, 0.1 M phosphate, pH 7.6. Corrected for the controls.

sults with casein as substrate (11), no significant differences in the optimum pH of the two chymotrypsins were observed with other substrates. Also in agreement with previous observations on casein (5), it was found that the end points of the reaction with the denatured substrates were the same for both chymotrypsins (Table 2).

The action of the two chymotrypsins was also compared on two samples of native lysozyme: one freshly prepared in this laboratory, the other obtained from Armour and Co. (Fig. 2). The freshly prepared lyso-

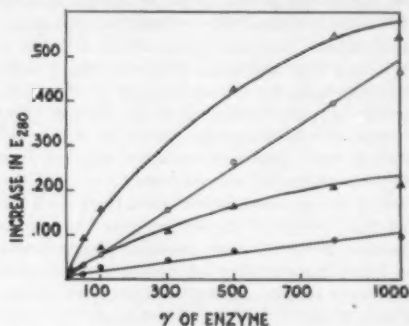


FIG. 2. —○—, Chymotrypsin α , native lysozyme freshly prepared; —●—, Chymotrypsin B, native lysozyme freshly prepared. —△—, Chymotrypsin α , native lysozyme, Armour and Co.; —▲—, Chymotrypsin B, native lysozyme, Armour and Co. Concentration of substrate E_{280} = 16.4, pH 7.6, phosphate buffer in all tubes. Incubation time, 20 min. All figures corrected for blanks.

zyme was more resistant to the action of both chymotrypsins and also showed the greatest difference in susceptibility to digestion by the two enzymes; chymotrypsin B accounted for only about 25% of the digestion obtained with chymotrypsin α .

According to Lindenstrom-Lang (12), the digestion of native proteins is preceded by denaturation. The experiment with lysozyme supports this interpretation. Furthermore, it suggests that chymotrypsin B differs from chymotrypsin α mainly in its denaturing ability.

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Comments and Communications

Religion and Higher Education

THE letter of John R. Sampey, published in the September 28, 1951, issue of *SCIENCE*, requires some qualifications concerning the use of the word "religion." Indeed, on the basis of the references quoted, it appears that not all church-controlled colleges do contribute significantly to the training of scientists. Among the 50 institutions listed by Knapp and Goodrich (1) none is related to, or controlled by, one of the oldest Christian religious groups. Table 2 in the same article shows that this same religious group controls colleges that have the lowest production of scientists.

Furthermore, the studies of R. K. Merton (2) and D. Stimson (3) show that the growth of science in the seventeenth and eighteenth centuries was not equally helped by the different religious traditions of the time.

It seems unwarranted to conclude from such observations that "religion" in general goes hand in hand with science. Before anyone can make such a generalization, many more studies will be required to evaluate the influences of the different religious traditions on the development of the scientific method.

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Rejuvenation Re-evaluated

ACCORDING to a dispatch dated Sept. 4, 1951, from Lausanne, Switzerland, Serge Voronoff—who, at the height of his career, was known as "The Great Rejuvenator"—died at the age of 85, not of senility, to be sure, but after suffering two heart attacks, the second of which was fatal. The Russian-born director of experimental surgery at the Collège de France, Paris, had once gained considerable fame by attempting to graft testicular and ovarian transplants from anthropoid apes into human beings.

Thanks to such a "gerontologie intervention," one of my elderly professors at the University of Nancy, it was rumored, had been retained on the faculty beyond retirement age. He used to report to work daily astride a bicycle, "so as to restore circulation in the parts concerned," he would say. Even the ex-Kaiser's sister, who had become infatuated with a much younger commoner, the waiter Zoubkov, gladly submitted to a *greffe* at Voronoff's hands.

The effect of such attempts were never very lasting, but now that surgical science has advanced, and we understand more about the factors influencing tissue growth and cicatrization, and about the role of hor-

mones, it is permissible to wonder whether the interspecific incompatibility could be overcome and the withering or resorption of transplants avoided. I still feel that Voronoff need not have met with so much skepticism and sarcasm when he arrived in this country shortly before World War II. He returned to Europe a broken and almost forgotten man. Perhaps I owe it posthumously to his memory to express my faith in the validity of some of his intraspecific animal experiments, at least. These were undertaken in collaboration with his brother Georges and with Dr. Dartigues, past president of the Société des Chirurgiens de Paris (1-4). As a student, I was privileged to witness the operative technique and to see several of the progeny that had been sired by previously infertile males.

The Voronoff method applicable to animal husbandry consists in grafting crescent-shaped portions of, say calf or lamb testicle into the testes of a sexually worn-out male of the same species (Fig. 1)—

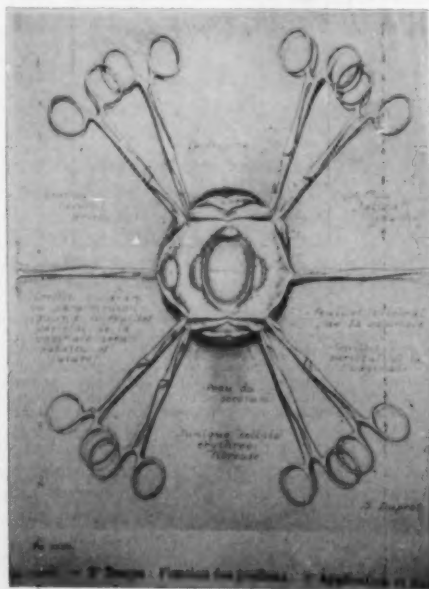


FIG. 1.

i.e., bull, ram, or other senile sire to be rejuvenated. The scion stimulates the production of testosterone and of viable spermatozoa by the subject's own testicular tissue. There is a detailed account of a number of more or less significant experiments that were performed in France, Italy, Algeria, and Brazil during the early 1920s in one of Voronoff's out-of-print publications that I am lucky enough to possess (5). We should not forget that the reported experiments were made 30 years too soon, when the expense involved

must have appeared excessive in relation to rejuvenating a bull for only a breeding season or two of effective service. Not so in our own era of artificial insemination and of egg implantation into foster mothers, when the reproductive power of a progenitor is spread over a much larger herd or flock.

Voronoff's method should prove of especially timely importance for prolonging the usefulness of high-priced livestock, which, shipped abroad under the various ECA, Point Four, and private (e.g., IBEC) programs of aid to underdeveloped countries, may become prematurely sterile in an adverse climatic environment.

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Potentiometric Measurements in Colloidal Systems

THE letter by Karol J. Mysels (1) in some ways clarifies the issues raised by Jenny *et al.* (2), yet in other respects it may cause further confusion. Dr. Mysels at the time of writing probably did not have available the detailed criticisms by Marshall (3), and by Peech and McDevitt (4) of a paper by Coleman, Williams, Neilson, and Jenny, entitled "On the Validity of Interpretations of Potentiometrically Measured Soil pH" (5).

It seems now to be agreed that a proper criterion as to the condition under which the KCl liquid junction potential is small is that the KCl solution shall be concentrated in comparison with the colloidal system (all contributing ions included). Thus, since saturated KCl (3.5 M) bridges are normally employed, we may dismiss from consideration all colloidal systems having ionic concentrations below, say, 0.1 molar. More concentrated systems, such as beds of granular cation exchange resins, call for special consideration. The Teorell-Meyer-Sievers theory can well be applied to such cases when a proper steady state has been reached (see below).

As Mysels points out, a crucial factor in concentrated colloidal systems is the contact with the KCl bridge. However, he seems to have missed one important aspect; namely, that the salt solution should make contact with a representative cross section of the system as a whole. Valid potentiometric interpretations depend greatly on this condition being fulfilled. Different results may readily be obtained in coarse granular systems, depending upon the kind of contact attained.

This was well illustrated here some months ago in

an experiment performed by Wm. J. Upchurch. A column of 60-mesh cation exchange resin IR 120 (potassium-saturated) was supported on a sintered glass filter disk. The pores of the latter were filled with saturated KCl solution, with a reservoir under the filter connected to a side tube. By raising the level of KCl in the side tube it could be brought into contact with a complete cross section of the exchanger. After this was done, a saturated calomel electrode was inserted in the side tube. Then a second saturated calomel electrode of the Beckman type was pushed into the upper part of the column of exchanger after the manner of Jenny *et al.* Thus we apparently had the simple system, Calomel | Sat. KCl | K Exchanger | Sat. KCl | Calomel, which of course should give zero potential under proper conditions. This Beckman type of electrode, however, furnishes KCl for the liquid junction by a very slow gravity flow down an asbestos fiber in a glass capillary. The conditions were evidently very far from ideal because a maximum potential of 35 mv was observed, which slowly came down to zero over a total time of 10 days.

When electrodes of improved design were employed, this time interval was greatly reduced; but any kind of small-bore, upturned tip that depends on diffusion to make contact requires hours for the true steady state to be reached. Granular systems thus require special design of the KCl junctions in order to give a truly representative contact in a short time.

Colloidal suspensions of particles $< 1\mu$ naturally do not cause difficulties of this order of magnitude. Nevertheless, instantaneous readings cannot always be relied upon, and the KCl should be given time to form a true boundary. In our experience 15–20 min amply suffice, where the KCl makes contact at the end of a well-defined tip of $\frac{1}{2}$ –2-mm cross section.

The "perched" potential at first obtained with the resin exchanger evidently includes the average work done in moving an ion from the granular system to a layer of water interposed between the KCl and the granules. Because the granular system contains water as well as resin this "perched" value does not represent the total phase potential of the resin against water; it will be somewhat less, depending on the porosity.

Finally, as regards the potentials to be expected when saturated KCl bridges come into true steady state contact with concentrated colloidal systems, the Meyer and Sievers theory indicates relatively low values compared with the phase potentials and "perched" potentials just discussed. If the effective cationic concentration A of the resin continuous phase is taken as equal to that of the ions in saturated KCl, then the Donnan potential according to the Meyer and Sievers theory is about 12 mv. Higher values than this could only arise if A effectively exceeded 3.5 M, and in view of the distribution of ionizing sites in exchange materials this would be barely possible. The liquid junction potential in the interior of the resin is proportional to the difference in mobility between the ions of the salt and can therefore be made

vanishingly small when the ions are equal in this respect. Thus with KCl the only potential of significance when a steady state boundary has been achieved is of the kind evaluated above.

The limiting case derived from the Meyer and Sievers theory by Mysels corresponds precisely to the experiment described above, which gave rise to the "perched" potential. The steady state potential between saturated KCl and any exchange material is likely to be much smaller.

Dr. Mysels' letter fulfills a useful purpose by drawing attention to the fact that we must make up our minds what kind of junction we are concerned with in any particular experiment. It seems to the writer that a junction with a representative cross section of the system under investigation is desirable. Conclusions drawn from such measured potentials refer then to the system as a whole. The colloid chemist's task, in general, is the interpretation of such systems.

C. EDMUND MARSHALL

Department of Soils, University of Missouri

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A Practical Laboratory Method for Mass Culturing Bacteria¹

BACTERIOLOGICAL investigations involving an elucidation of the chemical constituents of bacteria are frequently impeded by lack of suitable facilities for growing sufficient quantities of cells. The method described below requires no unusual laboratory apparatus, and it is mobile, inexpensive to construct, and applicable to mass cultivation of a variety of microorganisms for research purposes. The method has been used here for the past two years for the cultivation of both pathogenic and nonpathogenic bacteria. Good yields have been realized in a minimum of time, without undesirable degenerative changes occurring in the cells, and with no environmental contamination.

The culture container is a 7-gal, cylindrical Pyrex jar resting on a rubber-cushioned sheet-iron base (Fig. 1). Four tierods project from the base through matching holes drilled in the $\frac{1}{4}$ " aluminum cover. The latter has a collar welded to its under surface around which is fitted a $\frac{1}{4}$ " rubber gasket. A tight seal around the lid is obtained by tightening the tierod nuts on top of the cover with a wrench.

The cover has holes suitably drilled in it to receive a mercury seal, air and alkali tubes, glass and calomel electrodes, thermoregulator (glass rod type), heating element (300-w Calrod), thermometer (25°-45° C), mercury manometer, and siphon tube, all mounted in rubber stoppers (Fig. 2). A housing consisting of a $2\frac{1}{2}$ " copper pipe nipple with flanges on either end

¹ This investigation was supported in part by a contract (No. 9-ONR-87,200) between the Office of Naval Research and the University of New Mexico.

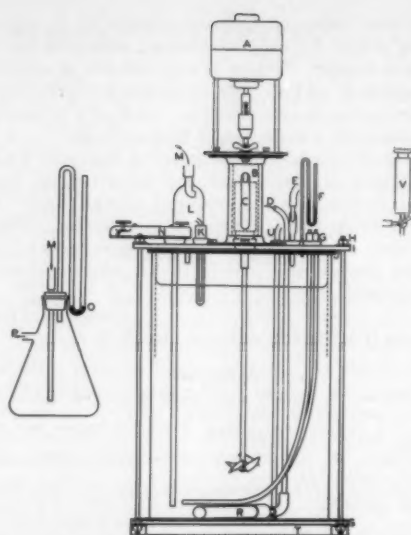


FIG. 1. Schematic representation of culture unit. A, motor; B, motor support; C, mercury seal; D, air "in" tube; E, to alkali reservoir; F, mercury manometer; G, heater; H, tierod cover nut; I, lid; J, rubber gasket; K, electrode; L, froth trap; M, exhaust air; N, thermoregulator; O, relief mercury manometer; P, to water pump; R, filter candle; S, rubber-cushioned base plate; T, wooden base; U, siphon tube (to sampler, for introduction of medium ingredients, for harvesting); V, sampler (30-ml syringe with 2-way Luer stopcock).

is bolted to the center of the cover to support the stirrer motor (1/20 hp, 1400 rpm). The latter is mounted as indicated (Fig. 2) to allow for proper alignment with the stainless steel stirrer through the mercury seal.

In operation, the thermometer and electrodes are sterilized separately in a quaternary ammonium salt and maintained in tubes of sterile broth. Cotton plugs are placed in the cover holes occupied by these, the motor removed, and the otherwise assembled apparatus is placed on its side in an ordinary autoclave and sterilized. After sterilization, the thermometer and electrodes are aseptically inserted into the cover, the motor attached, and the proper amounts (about 24

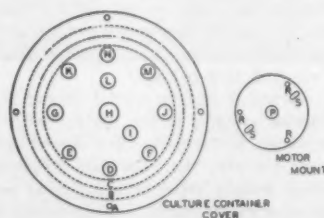


FIG. 2. Culture container cover. B, rubber gasket; C, collar; holes for: A, tierods; D, E, electrodes; F, air out; G, heater; H, mercury seal; J, manometer; K, siphon; L, alkali; N, thermometer; M, thermoregulator. Motor mount: R, taped holes for leveling screws; S, slots for motor mount bolts; P, drilled holes for stirrer shaft.

liters) of distilled water previously sterilized and stored in 5-gal carboys, along with sterilized concentrates of the medium ingredients, are aseptically siphoned into the container.

The pH of the medium is initially adjusted and maintained during the growth of the culture by connecting the electrodes to an a-c pH meter and, with constant stirring, by manually adjusting the rate of addition of alkali. The incubation temperature is held to within $\pm 0.1^\circ \text{C}$ with the thermoregulator indicated, without the necessity of interposing a relay system.

Aeration is obtained by forcing compressed air through a filter candle while the exhaust air is aspirated from the container with a water pump at the same time. The rates of the air flow are balanced to maintain a slight negative pressure within the apparatus, obviating any chance of environmental con-

tamination. A relief mercury manometer adjusts for fluctuation in water flow and compressed air pressure, as shown. The addition of an antifoam reagent such as *n*-butyl phosphate prevents undue foaming. At the termination of incubation, the culture may be easily harvested by siphoning it directly into a masked Sharples Supercentrifuge.

With this apparatus, we obtain yields of 55 g, dry weight, of *Shigella sonnei* organisms in $7\frac{1}{2}$ hr, using a simple culture medium containing 1% dextrose as fermentable sugar. About 470 ml of 5 *N* NaOH solution is required to maintain neutrality during the incubation period.

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²The technical assistance given by Philip G. Crook is gratefully acknowledged.

Book Reviews

Combustion, Flames and Explosions of Gases.

Bernard Lewis and Guenther von Elbe. New York: Academic Press, 1951. 795 pp. \$13.50.

In recent years, the original book entitled *Combustion, Flames and Explosions of Gases*, issued by Cambridge University Press in 1938, achieved ultimate literary distinction by disappearing from library shelves—the copies apparently going into bookcases of prospective purchasers who were unable to obtain them by other means.

The publication of this second book by Lewis and von Elbe has been anticipated with interest by workers in combustion research. The authors, who are associated with the Explosives and Physical Sciences Division, U. S. Bureau of Mines, are eminently qualified by years of work on combustion to write a comprehensive text on the subject.

Although the authors borrowed the title of their first treatise, the tremendous increase in the scope and volume of combustion research in the past decade required that they write essentially a new book. It is intended to provide the investigator, whether he be research scientist, industrial engineer, or student, with the fundamental observations and theories concerning combustion.

This book, like its predecessor, is in four parts. The first discusses the chemistry and kinetics of combustion reactions. New material on reactions of oxygen with hydrogen, carbon monoxide, and hydrocarbons is given. The second part, covering flame propagation, shows the greatest expansion of knowledge. Chapters on flame photography and pressure recording, combustion in nonturbulent and turbulent gases, fuel jets, burners, detonation waves, and flames in electric fields are included.

Part III concerns experimental and theoretical in-

vestigations of adiabatic explosions for several systems. It is essentially unchanged from the corresponding section in the first book. Part IV covers technical combustion processes. New material on gas turbines and turbojets is included. The appendices list selected thermodynamic data, limits of inflammability, and flame temperatures.

The presence of this book on the desk of the combustion investigator is justified alone by its extensive reference list of more than 800 authors, its abundant descriptions of experimental techniques, and its compilations of data. In addition the authors give detailed expositions of many current theories.

The only adverse criticism this reviewer is disposed to make is that the research of several workers has been omitted. Some of the omitted work may have been published after the literature survey was completed. This criticism, then, only indicates the fate of a book in an ever-expanding field. Undoubtedly 13 years hence we shall look to the authors for a third volume in their series.

MARJORIE W. EVANS

Armour Research Foundation, Chicago, Illinois

Igneous and Metamorphic Petrology. Francis J.

Turner and Jean Verhoogen. New York: McGraw-Hill, 1951. 602 pp. \$9.00.

Seldom has there been a book published that can be recommended so highly as this impressive volume. Although it is intended for the use of advanced students, research workers, and teachers in the field of geology, it is essential collateral reading for serious students in all branches of the natural and physical sciences who have an interest in the earth and in the physical and chemical principles that underlie rock genesis. It provides factual information on the classi-

fication, composition, and origin of the igneous rocks and on their subsequent modification in response to changing thermodynamic environment in the earth's surface to a depth of 15 or 20 km.

In this rigorous advanced treatise, the underlying principles of phase equilibrium, the physicochemical behavior of rock-forming minerals as determined by laboratory experiment and as deduced from thermodynamic theory, and the data on the igneous and metamorphic rocks from geological field evidence are presented, correlated, and interpreted in a straightforward, lucid, and convincing manner. The complexities involved in the behavior of multicomponent systems under a wide range of changing physical conditions form the theoretical and quantitative background for the discussion of both igneous and metamorphic phenomena which, in a most unusual approach, are treated and interpreted against the same common principles.

The general plan of the book is sixfold: (1) An introduction that presents the principles of chemical equilibrium and thermodynamics, briefly discusses rock classification with the details reduced to a minimum, then presents igneous rock associations and the concept of petrographic provinces, followed by a presentation of factual information derived from laboratory studies of silicate melts. (2) A discussion and interpretation of the igneous rocks that include the crystallization of basaltic and granitic magmas, the reaction series, oceanic volcanic associations, non-orogenic continental volcanic regions with alkaline or plateau basalt affinities, volcanic associations of orogenic regions, plutonic rock associations, the calc-alkaline series, alkaline rocks, and those rocks that are high in volatiles. (3) A presentation of the constitution of the earth with a discussion of the environment, origin, and evolution of magmas. (4) An introduction to metamorphism that includes classification and the principles governing the chemical adjustment of solid rocks to metamorphic conditions. (5) A discussion and interpretation of metamorphic rocks, zones, and facies, of chemical changes, and of fabric. (6) A presentation and interpretation of the relations of metamorphism to magma and orogeny, with discussions of both regional and contact metamorphism.

This excellent treatise should be in every scientific library and on the reference shelf of every teacher and advanced student in geology.

Geophysical Laboratory
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J. F. SCHAIER

Smithsonian Meteorological Tables. 6th rev. ed.

Compiled by Robert J. List. Washington, D. C.: Smithsonian Inst., 1951. 527 pp. \$4.00.

This edition of the well-known Smithsonian publication is the first postwar revision; it replaces the fifth edition published in 1939. Although larger (58 new tables and 159 additional pages) than the former edition, it is not merely an expansion. Before noting

the changes, it may be well to summarize the contents.

After a brief introduction, the book contains lists of tables under the categories: "Conversion Tables;" "Wind and Dynamical Tables;" "Barometric and Hypsometric Tables;" "Geopotential and Aerological Tables;" "Standard Atmosphere and Altimetry Tables;" "Thermodynamic Tables;" "Hygrometric and Psychrometric Tables;" "Tables of Miscellaneous Physical Properties of Air and Air-borne Particles;" "Tables of Miscellaneous Properties of Water Substance and Soils;" "Radiation and Visibility Tables;" and "Geodetic and Astronomical Tables." This listing is evidence of some of the changes that have been made. For example, the new edition does not list meteorological stations (such a list occupied 31 pages of the former edition); nor does it list meteorological codes. Certain other deletions have been made, most of them good. For example, the thermometric table correcting for the temperature of the emergent mercurial column is gone. Such a table is appropriate in physics or chemistry tables but is not needed in meteorology, where the bulb and column of a thermometer will generally be at the same temperature.

The page gain resulting from the deletions and the added pages has been utilized both for the presentation of new tables and for the expansion of old ones. Obvious changes are those resulting from our increased interest and work with the upper air—the addition of standard atmosphere tables and an increased number of radiation tables. Extensions of old tables include the expansion of the range of speed tables to yield directly conversions of speeds up to 400 mph. Other revisions are those that take into account recent definitions adopted by the IMO. For example, the Beaufort scale has been extended beyond force 12. Perhaps a more important example is the use of the new definition of relative humidity (in terms of the ratio of actual to saturation mixing ratios rather than of actual to saturation vapor pressures).

A minor criticism is the failure of the compilers to adopt the meter ton second system. It is not overly important which system of units meteorologists use, but it would be convenient if they all chose the same one. Since the IMO in 1911 adopted the mts system, it might well have been utilized for these tables.

The arrangement of tables and their explanations has been altered and, I believe, improved in balance. In place of the older system in which the explanations of the various tables were concentrated in the first 86 pages, in the new edition the explanations are placed throughout the book, each near to, and often on the same page as, the table to which it refers.

This edition represents a useful updating, in terms of wartime and postwar developments in meteorology, of a standard reference work. The resulting gain in usefulness will be important to any user.

LEON SHERMAN

Department of Meteorology
Florida State University

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SYMPOSIUM on RADIOBIOLOGY

The BASIC ASPECTS of RADIATION EFFECTS on LIVING SYSTEMS

Edited by JAMES J. NICKSON, *Cornell University School of Medicine*, this new publication is the outgrowth of the Symposium on Radiobiology, sponsored by the National Research Council, assisted by the Atomic Energy Commission and the Office of Naval Research, and held at Oberlin College in 1950. Specialists in all fields related to radiobiology described recent advances and summarized the present state of knowledge in their own fields. These experts concentrated on the basic aspects of radiation effects on living cells—"It appeared desirable to avoid numerous subdivisions in order to facilitate the handling of this problem. The committee concluded, therefore, that it should first center on the simplest living unit—the cell—and then transfer directly to a complex living system. The mammalian organism, which would in almost all circumstances be our eventual target, was therefore chosen." April 1952. Approx. 475 pages. Prob. \$4.00.

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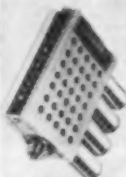
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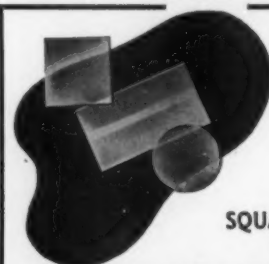
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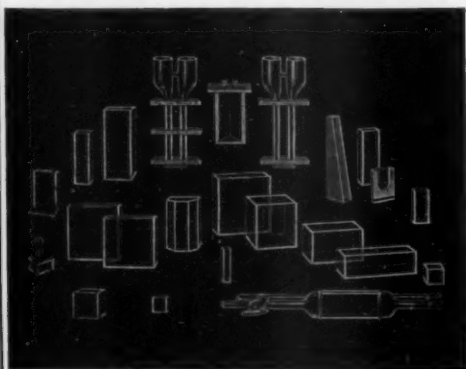
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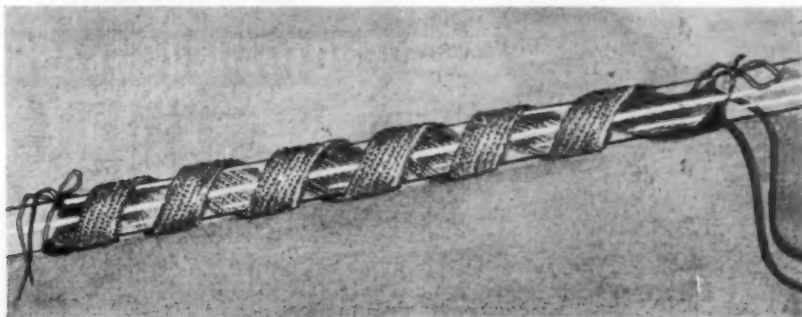
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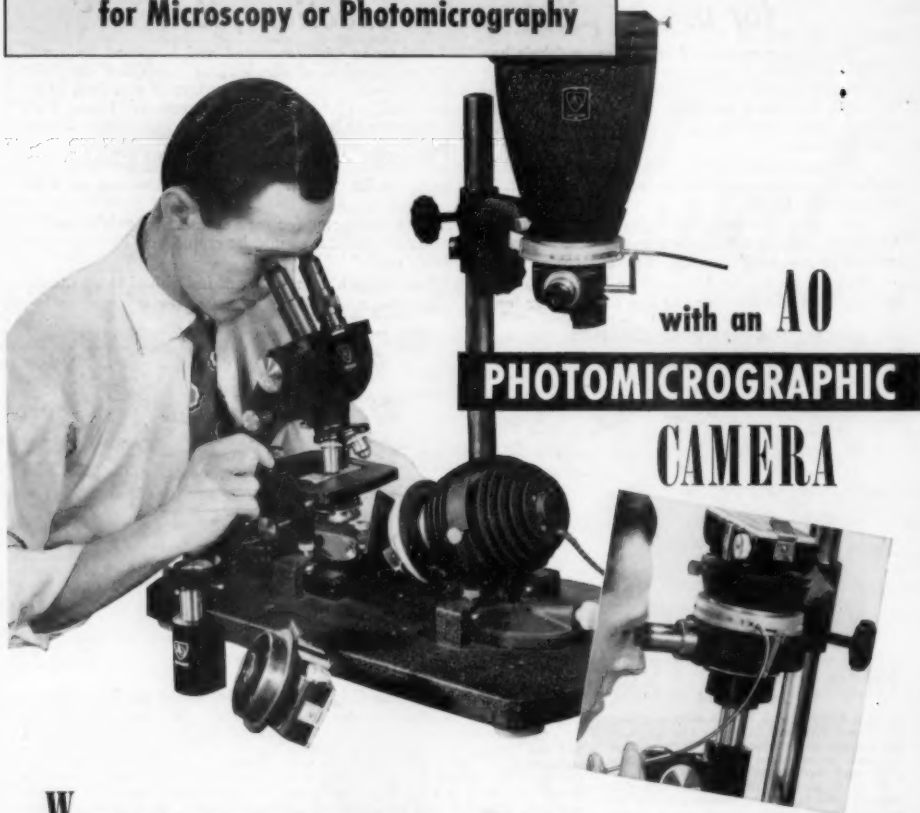
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